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BIOENERGETICS AND GROWTH

With Special Reference to the Efficiency Complex in Domestic Animals

BY

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Foreword

This volume presents an integration of the results of the researches sponsored by the Herman Frasch Foundation for Research in Agricultural Chemistry at the Missouri Agricultural Experiment Station. The major purpose of these investigations was to make a comparative study of the energetic efficiencies of agricultural processes, such as those concerned in the production of meat, milk, eggs, and muscular work, along with the factors influencing these efficiencies. The field is a very broad one and the discussions in this volume range over a wide territory. They include such important considerations as the energy cost of maintaining animals, of transforming feed into body tissue, milk, eggs, and other desired products, the relation of the speed with which the transformations occur to the efficiency of the process, the influence of the size of the producing animal on the efficiency and profit of the productive enterprise, and the influence of the rate of the process on the rate of aging. Many of the factors influencing efficiency, such as enzymes, minerals, vitamins, and hormones, are analyzed, largely with the aid of available literature.

The broad research project, the results of which are reported herein, was an institutional enterprise involving the cooperation of four departments in the Missouri Agricultural Experiment Station,—Dairy Husbandry, Animal Husbandry, Poultry Husbandry, and Agricultural Chemistry. The chairmen of these respective departments—A. C. Ragsdale, E. A. Trowbridge, H. L. Kempster, and A. G. Hogan—constituted the research committee, with the author of this volume serving as leader. The research plan was organized under the direction of Dean F. B. Mumford, who was Director of the Missouri Agricultural Experiment Station during most of the period of this investigation.

Many technical aspects of this research have been published as research bulletins of the Missouri Station and as technical articles in scientific journals. This volume brings together in integrated form the essential material incorporated in these many publications, along with much additional material brought together by the author.

The Frasch Foundation and its technical adviser, The American Chemical Society, working through its trustee, The United States Trust Company of New York, was represented on this research project during part of this period by Dr. R. W. Thatcher, distinguished agricultural chemist and president of the Massachusetts State College of Agriculture. Most of the long-range bioenergetic plans were formulated with Dr. Thatcher's advice and encouragement. Following Dr. Thatcher's death, this position was ably filled by two other representatives of Land Grant College staffs—first, by Dr. F. J. Sievers, Director of the Massachusetts Agricultural Experiment Station, and later by Dr. H. R. Kraybill, Head of the Department of Agricultural Chemistry of Purdue University. Dr. Kraybill has organized the plan through which the publication of the book was made possible.

This volume provides an excellent example of the results of a cooperative effort between an important private Foundation interested in the field of agriculture and an Agricultural Experiment Station associated with one of the Land Grant Colleges. The success of this cooperative endeavor in the development of a large volume of valuable research data and in its publication for general use, offers encouragement for similar plans of cooperation in the future.

The author desires to express his grateful appreciation to the Guggenheim Foundation for a European traveling Fellowship in connection with the preparation of this volume.

M. F. Miller, *Director*,
Missouri Agricultural Experiment Station

Columbia, Mo.,
November, 1944.

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Chapter 1

Introduction: Factors in the Efficiency Complex

> The situation is complicated and its difficulties are enhanced by the impossibility of saying everything at once. *J. H. Woodger*

> Ascertainable truth is piece-meal, partial, uncertain, and difficult. *B. Russell*

The efficiency complex involves innumerable genetic and environmental, as well as physiologic and economic factors. This book represents an attempt to integrate some physiologic and economic factors influencing efficiency with special reference to investigations with which the writer has been associated. Special attention is called to the operation of the principles of diminishing returns, limiting factors[1], and organismic interrelations and compensations in the efficiency complex. Much of the subject matter under consideration is, frankly, not applicable to the operation of an agricultural enterprise. But such apparently impracticable investigations are extremely important, partly because they "have dignified the calling of agriculture and have given the farmer an intellectual background and basis for his thinking that cannot be easily measured"[2].

1.1: Efficiency and profit, immediate and long-range. The animal husbandman, by employing special techniques, finds it possible to accelerate the speed of growth, milk production, egg production, and muscular work, of his animals. Whether this increased productivity results in greater *immediate* energetic efficiency, of course, depends on the relative acceleration of the productive processes on the one hand and maintenance cost on the other. But supposing that an increase in immediate energetic efficiency occurs, how will this affect the future health, fertility, and longevity (factors in *long-range* efficiency) of the animal? How do successive production increments compare with successive immediate and long-range cost increments? Obviously, the efficiency complex must be viewed from four standpoints: that of the animal and that of the animal husbandman, that of immediate efficiency and that of long-range efficiency.

---

[1] Cf. Blackman, F. F., *Ann. Bot.*, **19**, 281 (1905); Liebig, J., "Die Chemie in ihrer Anwendung auf Agrikultur", 1876.

[2] Mumford, F. B., "Fifty years of Agricultural Experiment Station Work". Address, Fiftieth Anniversary Exercises, University of Missouri, Agricultural Experiment Station, Columbia, June 21, 1938.

Energetic efficiency is the ratio of the desired form of output energy to the given form of input energy. In animals, the desired form of output energy is milk, meat, eggs, muscular work, wool, and so on; the input is a given category of feed energy, such as gross feed energy, digestible feed energy, metabolizable feed energy, net feed energy. *Gross efficiency** is the percentage of the energy in the given feed category, *inclusive of maintenance*, recovered in the desired product; *net efficiency*† is the percentage of the energy in the given feed category, *exclusive of maintenance*, recovered in the desired product.

But the problem does not end with *energetic efficiency. Monetary profit* offers a further and very substantial complication. Two 800-lb cows producing milk at the same energetic efficiency as one 1600-lb cow are not as profitable commercially. This is because the labor cost of milking, feeding, cleaning, housing, bookkeeping, etc., is nearly twice as great for two 800-lb cows as for one equally efficient 1600-lb cow, and the profit will be correspondingly less for the two small than for the one large cow. Energetic efficiency of milk production is a biologic index of "dairy merit", probably independent of body weight as such: rats, goats, and cows probably produce milk equally efficiently[3] but not equally profitably (see Chs. 3 and 22). Profit is dependent not only on energetic efficiency—a biologic characteristic—but also on many other factors, including labor and other overhead costs per unit of milk production, which are in turn dependent on size of animal and other factors. Similar problems are involved in producing meat, eggs, wool, muscular work, and so on.

1.2: Growth, form, and function. Growth is the basis of and closely related to many productive agricultural processes. Egg, milk, fat, and wool production are special types of, or closely related to, growth. The function of an animal is, furthermore, related to its *form*, the development of which is a growth phenomenon. Growth, form, and function (*e.g.*, the production of meat, milk, eggs) are closely interrelated, and special emphasis has been given to various aspects of growth phenomena (Chs. 16 to 20).

1.3: Organizational energy or the energy expended for the "work" of growth and morphogenesis. One expense of the overall or gross productive cost is the transformation of the original feed into the final productive *precursors*, circulating in the blood stream, or in temporary storage in the body. But there must be another expense, that of transforming the relatively simple, amorphous precursors, or building stones, into the complexly organized and

---

$$\text{* Gross efficiency} = \frac{\text{output energy (of milk, eggs, meat, work, etc.)}}{\text{input energy (of gross energy, TDN, etc.)}} \qquad (1.1)$$

The term "gross" is preferred to "total" efficiency in order to avoid the implication that we are dealing with "total" energy changes.

$$\text{† Net efficiency} = \frac{\text{output energy}}{\text{input energy less maintenance energy}} \qquad (1.2)$$

The term "net" is preferred to "partial" because of the well established usage for "net" (all reactions and efficiencies are partial).

[3] Brody, S., *J. Nut.*, **17**, 235 (1939).

thermodynamically rather improbable living organisms and related biologic products. This assumed energy cost of morphogenetic "work" may conceivably be of several different categories. First comes to mind potential or "structured" energy, analogous to the energy "structured" into a spring on winding it, or into a storage cell on charging it. The biologist's "action current", and indeed the whole field of electrophysiology, as well as muscular exercise (contraction and relaxation), is based on such charge-discharge phenomena. Bergson[4] and Terroine and Wurmser[5,6] suggested that the configuration of the formed tissue is on a different energetic level from that of the building-stone precursors.

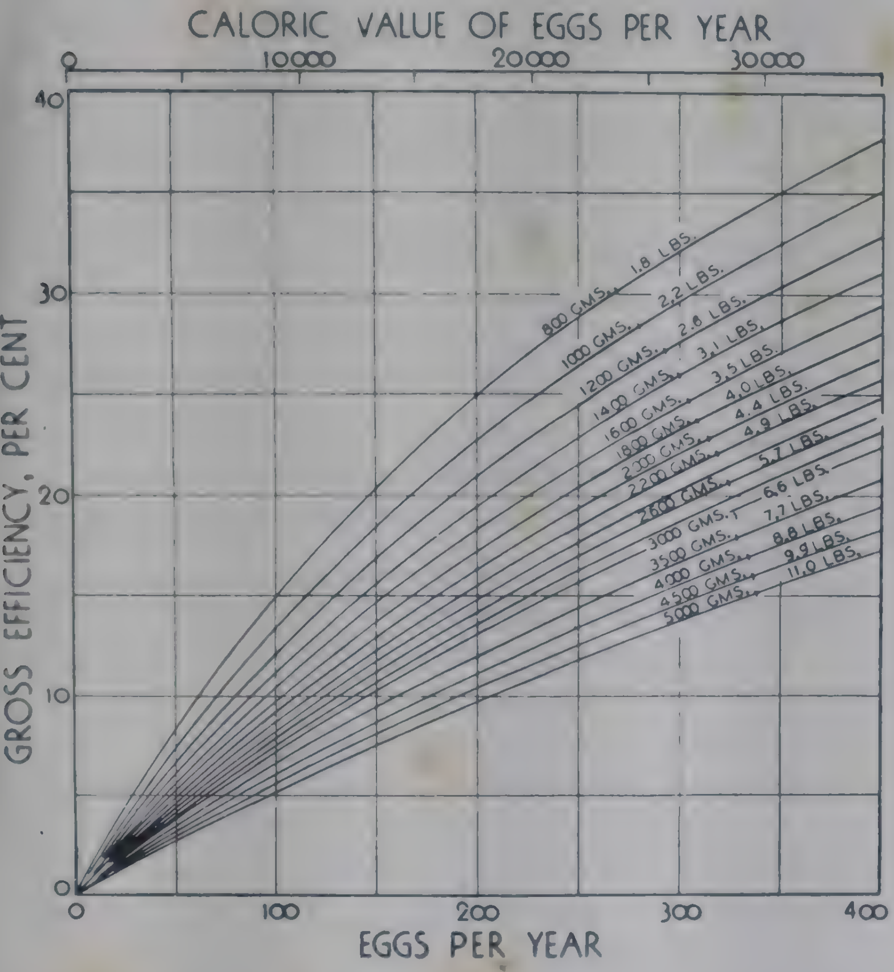

Fig. 1.1—Gross energetic efficiency of egg production for fowl of different body weight and different production levels, illustrating the operation of the principle of diminishing returns (Ch. 5).

---

[4] Two orders of phenomena are observed in living tissues, *anagenesis* and *katagenesis*. The role of the anagenetic energies is to raise the inferior energies to their own level by assimilating inorganic substances. Henri Bergson, "Creative Evolution", 1907.

[5] Pour édifier son organisme et le développer, il doit en méme temps exercer un travail contre l'éxtérieur et surtout dans la plupart des cas élever le potential chimique des substances dont il dispose. Il y a donc le besoin d'énergie. Terroine, E., and Wurmser, R., "L'énergie de croissance. I. Le développement de l'Aspergillus niger". *Bull. Soc. Chim. Biol.*, **4**, 519 (1922).

[6] (Cf. Bohr, C., and Hasselbalch, K. A., "Ueber die Kohlensaure production der Huhnerembroys", *Skand. Arch. physiol.*, **10**, 149 (1900); "Ueber die Warmeproduction und den Stoffwechsel des Embryos", *Id.*, **14**, 398 (1903). Tangl, F., "Beitrage zur energetik der ontogenese", *Pfl. Arch.*, **93**, 327; **98**, 475 (1903); **104**, 624 (1904); **121**, 347 (1908); **130**, 1, 55 (1909). Joseph Needham, "Chemical Embryology", Cambridge, 1931.

Next comes to mind an example of energy expenditure as is associated with the work of rearranging furniture. Such work is immediately paid for, to entropy, by dissipation of heat to the environment. The potential energy of the room is not increased by such work.

This problem of organization energy is fascinating in its obscurity and controversial implications, physicochemical, biological, and even theological, or metaphysical[7]. It cannot be put to a direct experimental test because, for the second assumption, it is not possible to separate or differentiate the heat of morphogenetic work from the heat of maintenance of the formed tissue[8]. This intriguing problem of organizational energy is discussed in some detail in Chapter 3.

1.4: Basal metabolism, maintenance cost, and efficiency. Living is an expensive process. Circulation, respiration, excretion, and muscle tension never cease while life remains, even under conditions of absolute rest. There are, moreover, energy wastes associated with inevitable activities of enzyme systems in their own right, independently of physiologic usefulness, and there is also an energy cost for maintaining the thermodynamically unstable living state (Ch. 3). These and related processes add up to the large energy cost of maintenance. The minimum energy cost (when the animal is at rest in a thermoneutral environment in the post-absorptive condition), called basal metabolism, is a popular subject for research. The *total maintenance* cost, as contrasted to *basal metabolism*, is not being investigated actively.

Because most feed consumed by animals is expended for basal metabolism and maintenance, we have given the problems considerable attention (especially in Chs. 13 to 15).

The following example illustrates an agriculturally practical aspect of organizational energy as well as of maintenance in relation to time, to energetic efficiency, and even to profit. We estimated mathematically (Ch. 23) that the *net* efficiency of egg production (not including maintenance cost) appears to be of the same order as the net efficiency of milk production; the *gross* efficiency (including maintenance cost, which is proportional to the time involved) of egg production, however, is only about half that of milk production. This difference in *gross* efficiency in the face of equal *net* efficiency may be explained by the greater structural complexity of egg (Ch. 23); there is required relatively more time and consequently relatively more maintenance energy to produce unit egg energy than unit milk energy. The periodic or cyclic nature of the egg-production process, in contrast to the continuous one of milk production, is another factor contributing to the lower gross energetic efficiency of egg production. This exemplifies how organizational complexity may condition in a practical way the gross efficiency of productive processes aside from the energy cost of morphogenesis, a more controversial problem (Ch. 3).

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[7] Bergson, *loc. cit.*, and his other books.

[8] Needham, *loc. cit.*; Tyler, A., *Pub. Staz. Zool. Napoli*, **13**, 155 (1933); *Quart. Rev. Biol.*, **17**, 197 (1942).

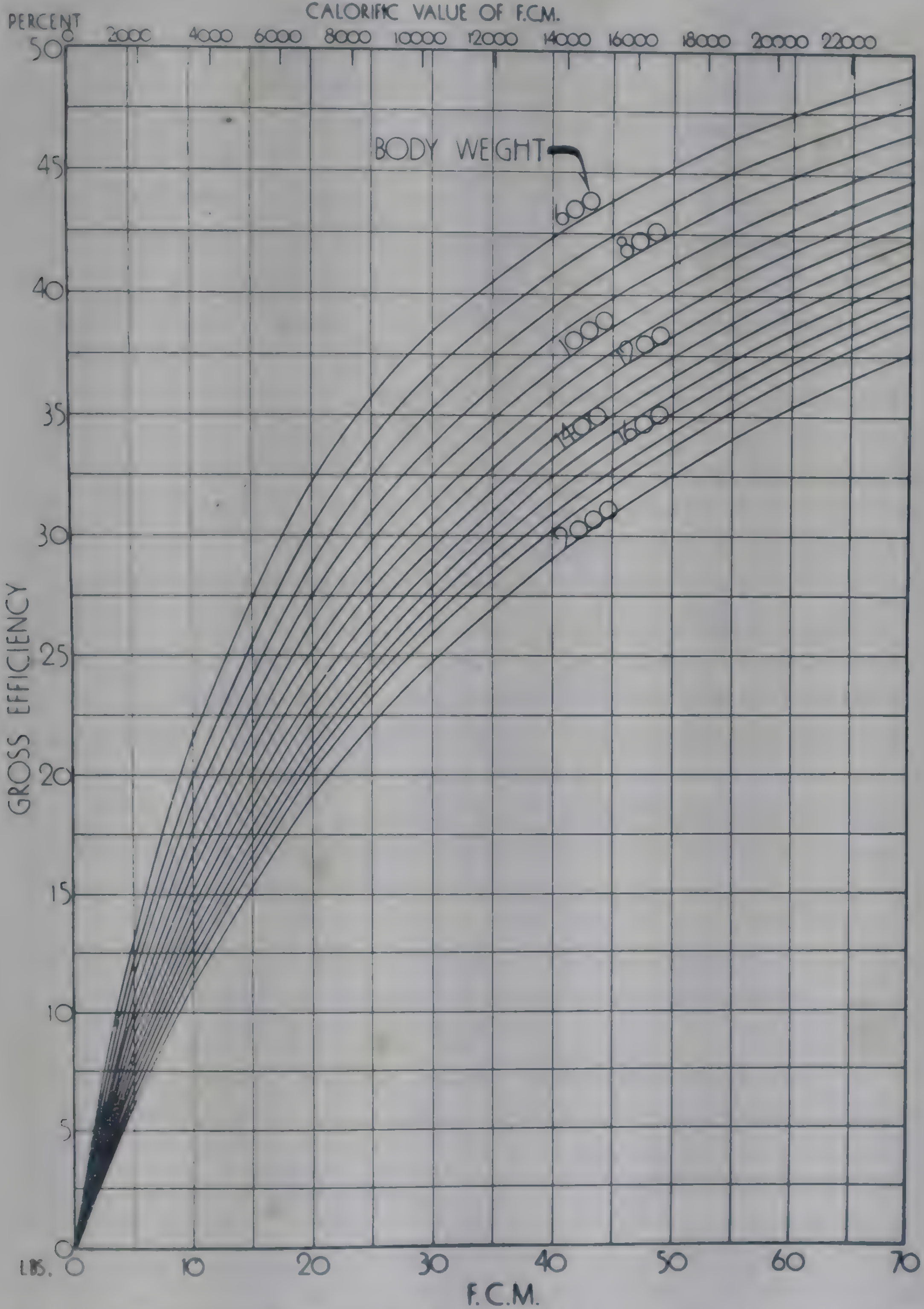

Fig. 1.2—Gross energetic efficiency of milk (F.C.M.) production for cattle of different body weight and different productive levels (see Sect. 5.4).

1.5: Nutritional categories. Productive processes transform input energy, which is food, or "feed" as it is called when used by farm animals, into desired products, milk, egg, meat, work, etc.

The transformation involves several steps. The feed (*gross-energy category**) undergoes digestion, and the digested material (*digestible-energy category*) enters the blood stream or storage organs. Undigested material and fermentation gases are eliminated from the alimentary canal. Some of the *digested nutrients* are eliminated by way of the kidneys; the remainder is *metabolizable energy*. Of the metabolizable energy, part is eliminated as heat increment of feeding ("specific dynamic action", referred to as SDA), the rest is the *net energy category*. Net energy is, then, that part of the total energy which is retained in the body for useful purposes, such as maintenance, growth, milk production, egg production, or muscular work. The fraction of feed energy eliminated in feces, urine, and SDA depends on the balance between nutrients (Ch. 20), on the plane of nutrition (Ch. 5), and on the animal's inherited ability to digest and utilize the feed.

1.6: Organismic and atomistic viewpoints. The energetic efficiency of productive processes depends on many interrelated factors. The specialist investigating one of these factors may be unfamiliar with the methods, aims, and literature of the others. The animal husbandman, however, is (theoretically) a student of the efficiency complex *as a whole*[9], because the animal is broader than any of the specialized or atomistic fields of knowledge.

The organism is particularly remarkable for its adaptive and regulative (homeostatic) devices adjusting it to fluctuating environmental conditions. Chapters 10 and 25 are concerned with some homeostatic or organismal devices and similar interrelations. Chapter 11 discusses an especially important homeostatic mechanism—body-temperature regulation—and the influence of environmental temperature on the efficiency of biological transformations.

The seasonal temperature rhythm is associated with the seasonal and diurnal light rhythms. Chapters 8 and 9 discuss the relation of these rhythms to productive processes.

Light not only furnishes energy to animals by way of the plant, but also catalyzes many productive processes. Other catalytic processes are discussed in Chapters 6 and 7.

There are individual differences in digestibility[10], metabolizability, and net-energy availability, with corresponding differences in the overall efficiency of the productive process. Of course, digestion itself is a very complex process in which innumerable factors participate, and it is possible that each of these factors is controlled by a separate gene or set of genes. "How many genes may be involved in the development of the reflex stimulating the salivary gland or the secretion of hydrochloric acid in the stomach!"[13] It is customary to overlook the variability of the individual factors and to conduct genetic investigations not on the ultimate factors but on complexes, such as inheritance of the complex "growth rate"[11], "milk production", "egg production", each of which is, of course, the resultant of innumerable interrelated inherited factors.

---

* The gross- and net-energy feed *categories* are not related to the gross and net *efficiencies* (equations 1.1 and 1.2).

[9] If anyone wishes to search out the truth of things in serious earnest, he ought not to select one special science; for all the sciences are conjoined with each other and interdependent. *Descartes*.

[10] Craft, W. A., and Willham, O. S., "Nutrition and genetics", *Proc. Am. Soc. Animal Production*, p. 260, Nov. 27-9, 1936.

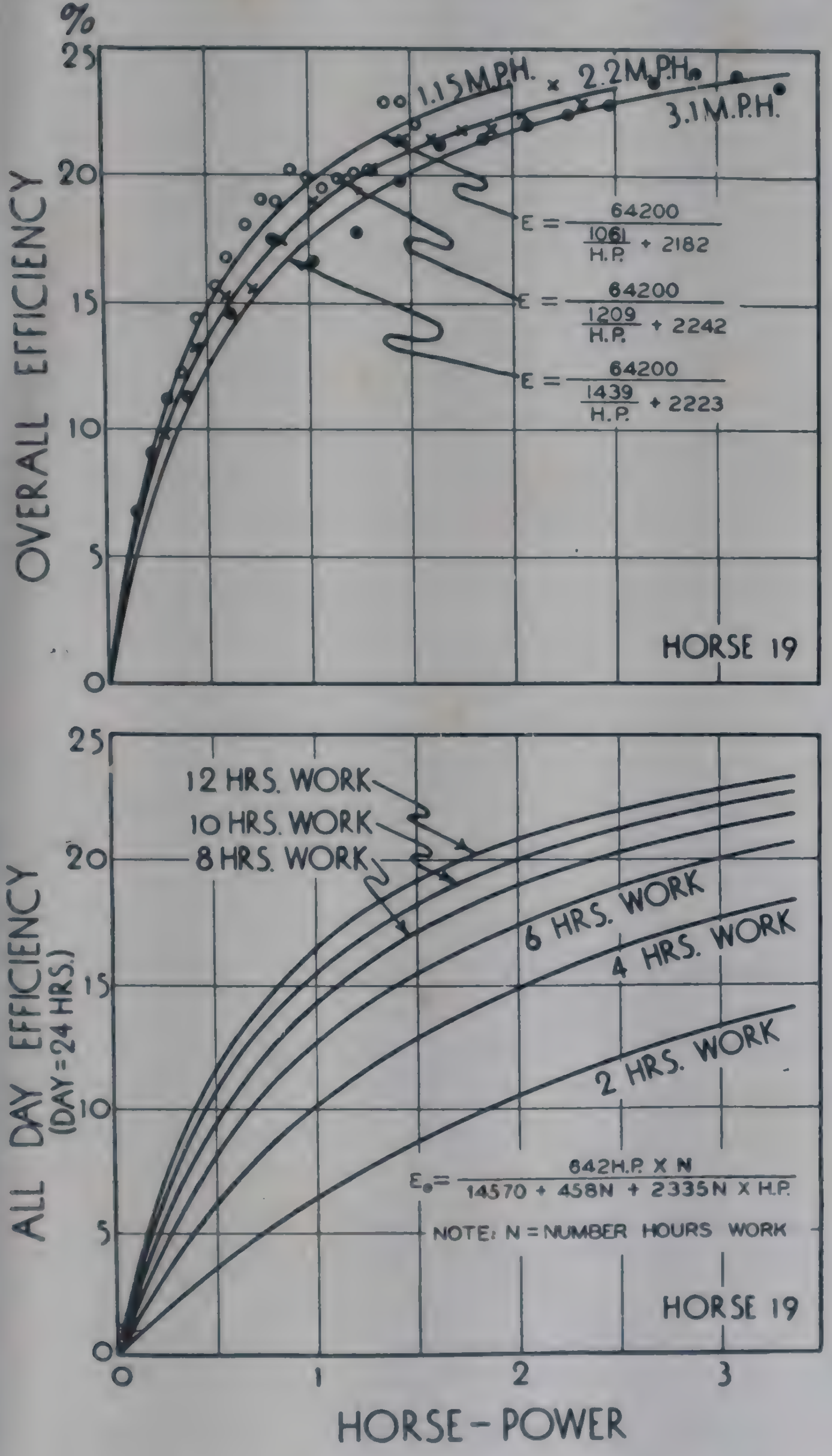

Fig. 1.3—Gross energetic efficiency for horses working at different rates, illustrating the operation of the principle of diminishing returns (Ch. 5).

The productive level is, by definition, directly proportional to the *net-energy* consumed above the maintenance level. It is not directly proportional to the *total feed* intake above the maintenance level, because digestibility, metabolizability, and net-energy availability of rations tend to decrease with the feed intake in accordance with the principle of diminishing increments (Ch. 5). Feed intake is, however, an excellent index of the productive aptitude of an animal[12], regardless of the nature of the productive process.[13] Indeed, there appears to be a good correlation[14] between growth rate in youth and milk-production rate at maturity (both being apparently correlated to the same extent with the feed consumption level); and dairy steers from high-milking dams fatten as efficiently as beef steers[15], high feed consumption being the common characteristic of both.

---

[11] Palmer, L. S., and Kennedy, C., "Food consumption and efficiency", *J. Biol. Chem.*, **90**, 545 (1931). Morris, H. P., Palmer, L. S., Kennedy, C., "Food requirements for the growth of the rat", Minnesota Agr. Exp. Sta. Technical Bull. 92, 1933.

High productivity is, rightly, sought for, but it should also be realized that it involves certain hazards. Thus, unusually high milk production may result in milk fever and related metabolic disorders, consequences of the inability of the digestive and assimilative systems to keep pace with the demands of the milk-producing apparatus. Long-range hazards of unusually high productive levels may be lessened resistance to infection, circulatory damage[16], and perhaps accelerated senescence (Ch. 18). Extreme muscular effort in hot weather is associated with relatively high mortality of horse and white man. (The less ambitious mule and colored man usually refuse to exert themselves unduly, with corresponding lower hot-weather mortality.)

The highly productive, and consequently highly efficient, animal is such because of a hereditary configuration in which all the participating efficiency factors are developed *harmoniously* for the given high production level. Relative overdevelopment or underdevelopment of one of the vitally participating factors may be catastrophic to the individual or even to the race. Mention was made of milk fever, increased susceptibility to infection, cardiac damage, and early senility as examples of possible hazards of unusually high rates of milk production under certain conditions; of high mortality of horses from "sun stroke" as result of hard muscular work in hot weather; and of high mortality of fowls as result of highly accelerated winter egg production by artificial lighting and feeding (Ch. 23) associated perhaps with nutritional deficiencies (Ch. 20). Other examples wil be cited presently (Ch. 7).

There are many individual peculiarities, genetic and environmental, affecting efficiency. Individual farm and laboratory animals—not to speak of humans—differ in their wisdom for selecting diets when offered free choice[17]. These may be hereditary or environmental. It is interesting to note that the growth rate of "superior" individuals is not maximum. By "superior" one[17] means those who are the most efficient users of food and have the highest livability. Contrary to the common belief, the most rapid growth is often associated with the highest early mortality[17]. Very rapid growth may be economical to the animal husbandman by saving overhead maintenance cost but not profitable to the animal whose longevity may be impaired thereby.

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[12] Eckles, C. H., and Reed, O. E., "Cause of wide variation in milk production". Univ. Mo. Ag. Exp. Sta. Res. Bull. 2, 1910.

[13] Kleiber, M., *Proc. Am. Soc. Animal Production*, Nov. 27–8, 1936.

[14] Prentice, E. P., *Hoard's Dairyman*, **81**, 120 (March 10, 1936).

[15] Winters, L. M., "Efficiency variations in steers", *Proc. Am. Soc. Animal Production*, (Nov. 7–8, 1936) and Minnesota Ag. Exp. Sta. Res. Bull. 94, 1933; Fuller, J. G., "The dairy breed steer in the feedlot", *Proc. Am. Soc. An. Prod.*, p. 88, (1930).

[16] Cf. Graham, W. R., Jr., *et al.*, *Proc. Roy. Soc.* **120B**, 330 (1936); *J. Nut.*, **7**, 407 (1934); *Am. J. Physiol.*, **122**, 150 (1938) who reported that one unit milk production is associated with 300 units of blood flow through the mammary gland. See also Sect. 21.4.3.

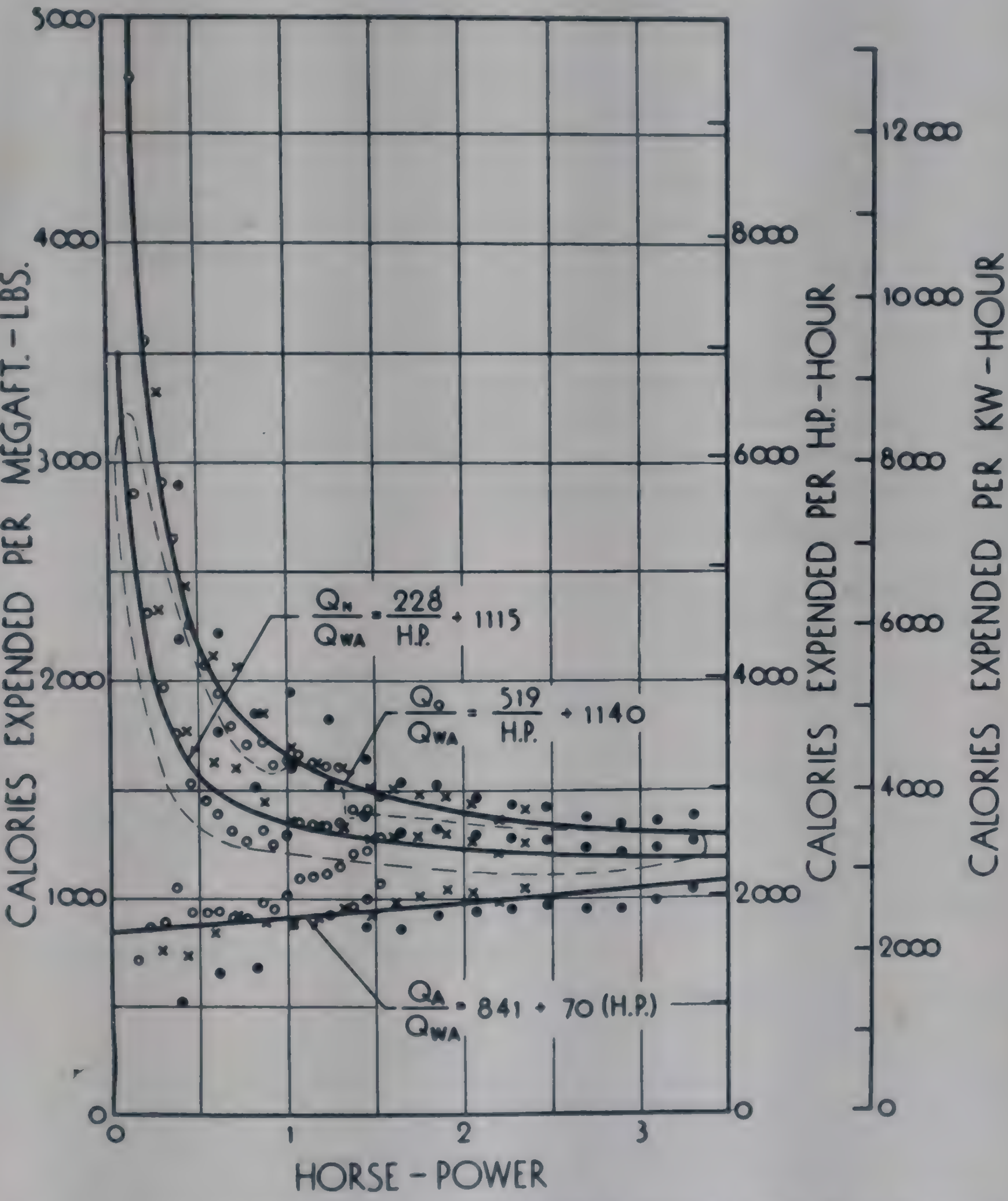

Fig. 1.4—Gross energetic efficiency, Q_0, expended per unit work, Q_{WA}, in horses at different work rates, approaching the absolute expense, Q_A, per unit work, Q_{WA}, as limit (see Ch. 24 for details).

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[17] Dove, W. F., *Am. Nat.*, **69**, 469 (1935); *Proc. Am. Soc. Animal Prod.*, p. 243 (Nov. 27, 1936); *J. Hered.*, **30**, 157 (1939). Maine Agr. Exp. Sta. Ann. Rep. for 1939, p. 727, also for 1938 and for 1935.

It is generally known that there are individual differences in susceptibility to rickets and to nutritional cataract[18], and to cancer induced by estrogens and carcinogens[19].

Neuro-psychiatric peculiarities offer another category of influences on the efficiency of productive processes. Thus animals vary in the amounts of energy they expend for activities un-related to the productive process. Rundquist[20] developed two strains of rats which differed in spontaneous activity. We are familiar with the fidgety horse, a "hard keeper", because he wastes so much energy on useless motion, and the placid horse, an "easy keeper". Some of these temperamental differences are due to endocrine peculiarities[21]. Skill in competitive sports, such as running, is, in part, a matter of eliminating useless motions, the result of training as well as heredity.

We thus end this chapter with the introductory statement that the efficiency complex involves innumerable genetic and environmental, physiologic, and economic factors with corresponding difficulties of integration enhanced by the impossibility of saying everything at once. We shall, therefore, break up our efficiency complex into its several components discussed in the following twenty-four chapters.

1.7: Appendix: The following summary of the efficiency equations will be useful as reference in future discussions.

$$\text{Gross* efficiency} = \frac{\text{energy output (as milk, eggs, meat, work)}}{\text{energy input (various categories of feed)}} \qquad (1.1)$$

$$\text{Net† efficiency} = \frac{\text{energy output}}{\text{energy input less maintenance energy}} \qquad (1.2)$$

Equation (1.1) may be expanded into its constituent components still further:

$$\begin{array}{l}\text{Gross}\\ \text{efficiency}\end{array} = \frac{\text{energy output}}{\begin{array}{l}\text{energy output + maintenance energy}\\ \qquad\qquad\text{+ other expenses in producing product}\end{array}} \qquad (1.3)$$

Equation 1.3 may be further expanded:

$$\begin{array}{l}\text{Overall or gross}\\ \text{energetic}\\ \text{efficiency}\end{array} = \frac{\text{energy output}}{\begin{array}{l}\text{energy of: (A) product + (B) maintenance + (C) ``work''}\\ \text{of organizing precursors into product + (D) increased me-}\\ \text{tabolism of productive system as result of its greater ac-}\\ \text{tivity and of whole body as result of higher hormone and}\\ \text{nutrient concentration in the blood + (E) wastes inci-}\\ \text{dental to transformation of precursors in blood to prod-}\\ \text{uct + (F) maintenance cost of growing product and so on.}\end{array}} \qquad (1.4)$$

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[18] Lambert, W. V., Ellis, N. R., Black, W. H., and Titus, H. W., *Proc. Am. Soc. Animal Production*, p. 236 (Nov. 1936).

[19] Allen, E., *J. Am. Med. Assn.*, **114**, 2107 (1940).

[20] Rundquist, E. A., "Inheritance of activity", *J. Comp. Psychol.*, **16**, 415 (1933).

[21] Cf. Hall, V. E., and Lindsay, M., "Spontaneous activity and the thyroid gland", *Endocrinology*, **22**, 66 (1938); Brody, E. B., *Id.*, **29**, 916 (1941).

* Gross energy *cost* of a process = cost including maintenance.

† Net energy *cost* = cost not including maintenance.

One might legitimately ask whether the "maintenance" of a productive animal includes item (D) in equation (1.4). The distinction in the denominator of equation (1.4), as between (C) and (F), and between (C) and (D) above, are necessarily arbitrary and subject to criticism, but they serve to illustrate the complexity of the situation.

The apparent efficiency will vary with the category of feed to which the product is compared. The computed efficiency will be greatest if the energy of the product is compared to the *net energy* of the feed, less if compared to *metabolizable energy*, still less if compared to *digestible energy*, and least if compared to gross energy.

While from the economic viewpoint the overall or gross efficiency [equation (1.1)] is all-important, from the theoretical viewpoint, the net efficiency [equation (1.2)] may be the more important, because it is not complicated by maintenance (not a part of the productive process), which is dependent on a miscellaneous array of extraneous factors. Because of the basic character of net efficiency, Terroine and Wurmser‡ termed it "rendement energetique réel", that is *real efficiency*, as contrasted to the overall or gross energetic efficiency which they termed "rendement energetique brut", that is *crude or apparent efficiency*. During growth, for example, the gross growth efficiency decreases with increasing age, perhaps not because the cost of organization increases, but because the amount of growth *in comparison to the size of the maintenance-expending body* decreases. The importance of the distinction between *gross* and *net* efficiency will become increasingly evident.

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‡ Terroine, E., and Wurmser, R., *loc. cit.*

Chapter 2

Energetics, Energy Units, and Dietary-Energy Categories[*]

> Science is the attempt to make the chaotic diversity of our sense-experience correspond to a logically uniform system of thought. *Albert Einstein*

2.1: Energetics. Bioenergetics, concerned with energy transformations in living things, is a branch of general energetics generalized by the first and second laws of thermodynamics. We shall discuss these briefly, and then attempt to extend the *thermodynamic form* treatment to the discussion of the several nutrient categories and wastes.

2.1.1: The first law[1], or the *principle of conservation of energy*, asserts that the total amount of energy in an isolated system remains constant. If energy appears at one place, an equal quantity of energy disappears simultaneously in another place; if energy disappears in one form, an equal quantity of energy appears simultaneously in another form. All known forms of energy (mechanical, electrical, magnetic, chemical, etc.) have been converted quantitatively into heat.

The *principle of conservation of matter* is another form of the principle of conservation of energy. Matter and energy are inseparable; according to the theory of relativity and to other considerations[2], matter and energy are different expressions or measures of the same thing, and they are frequently hyphenated in writing, as *energy-matter*.

The first law is not concerned with mechanisms or rates of energy changes, but only with the initial and final energetic states of the system. It holds true for living as well as for non-living systems: the energy equivalent of work performed by an animal, plus the maintenance energy of the animal, plus the heat increment of feeding must equal the energy generated from the oxidation of nutrients. This definiteness gives the first law a sense of universal finality, and a firm basis for bioenergetic investigations even if the mechanisms of the reactions are unknown.

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[*] Grateful acknowledgments are made to Allen E. Stearn, Professor of Physical Chemistry, University of Missouri, for valuable suggestions and for reading the manuscript; also to ProfessorsHenry E. Bent and Earl A. Long of the same department for valuable suggestions.

[1] This first law may be said to have been conceived by Lavoisier, "the father of the science of nutrition", but formulated by Robert Julius Mayer (a physician) in 1842, Herman Helmholtz (a physiologist) in 1847, and substantiated experimentally by James Prescott Joule (a brewer) in 1843 who determined the mechanical equivalent of heat. It is curious that this great generalization of physics is not due to professional physicists: physicists "were tired of futile generalities and anxious to make amends for the wasted time by conscientious factual research" (Epstein, P. S., "Textbook of Thermodynamics", pp. 27-34, 1937

[2] Lewis, G. N., *Science*, **30**, 84 (1909). The relation between energy, E, and rest mass, m, is given by the equation $E = mC^2$, in which C is the velocity of light.

The first law is usually represented by the equation

$$\Delta E = q - w \tag{2.1}$$

in which ΔE represents increase in the energy content of the system which is equal to q, the heat absorbed from the surroundings (when its sign is positive and heat evolved by the system when its sign is negative), less w, the work done by the system upon the surroundings[3].

When work is performed isothermally, $\Delta E = -w$; when heat is transferred without work, $\Delta E = q$.

The concept of change in *energy* content, ΔE, is usually employed when gases are involved at *constant volume*. At *constant pressure*, it is customary to employ the concept change in *heat* content, ΔH, when equation (2.1) is written

$$\Delta H = q - w \tag{2.1a}$$

For reactions not involving gases, the valus of ΔE and ΔH are equal. For reactions involving gases,

$$\Delta H = \Delta E + RT\Delta n = \Delta E + 1.988T\Delta n$$

in which n represents number of mols of the gas, and $R = 1.988$ Cal/°C.

Biologists employ ΔH rather than ΔE because their observations and methods involve constant pressure.

When a reaction occurs reversibly, w is *maximal work*, and ΔE or ΔH is the latent heat of the reaction.

A reaction is said to be *reversible* when it proceeds from stage A to the subsequent stage B in such manner that the energy change is just enough to permit the reversal back from stage B to stage A without loss of energy. When other conditions do not enter to change a situation, natural processes are probably never reversible. This concept of reversibility is, nevertheless, very important in the elucidation of thermodynamic theory, and in man-made system changes, such as in the slow-charging-discharging standard cadmium cell, the concept of reversibility is virtually realized in practice.

As regards the applicability of the first law to animals, many contributions were made beginning with Lavoisier[4], to whom the modern concept of animal heat is attributed, in 1777, long before the law was formulated. The proof of the applicability of the first law to animals (dogs) is, however, attributed to Rubner[5], confirmed (on man, working, riding a bicycle) by Atwater and Benedict[6], and (on cattle) by Armsby[7].

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[3] The notations are after Lewis, G. N., and Randall, M., "Thermodynamics", McGraw-Hill Book Co., 1923.

[4] Lavoisier, A. L., "Expériences sur la respiration des animaux et sur les changements qui arrivent à l'air en passant par leur poumons", Mém. de l'Académie de Science, (1777) p. 185. Lavoisier and Laplace, P. S., *Id.* (1780) p. 379. Lavoisier and Seguin, *Id.* (1789) p. 566.

[5] Rubner, M., "Calorimetrische Untersuchungen", *Z. Biol.*, **21**, 250, 337 (1885); **30**, 73 (1894). For the history, see Rubner "Die Gesetze des Energieverbrauchs bei der Ernährung", Leipzig, 1902, and Lusk, G., "The Science of Nutrition", Philadelphia, 1928.

[6] Atwater, W. O., and Benedict, F. G., "The Metabolism of Matter and Energy in the Human Body", U. S. Dept. Agr. Bull. 136, 1903.

[7] Armsby, H. P., "Principles of Animal Nutrition", New York, 1903 and following editions.

The proof consists in comparing the heat of oxidation of nutrients outside and within the body. Outside the body the heat of combustion, ΔH, is determined with an ordinary calorimeter. Within the body, the *nature* of nutrients (carbohydrates, fats, proteins) oxidized is determined from the respiratory quotient and urinary nitrogen (Ch. 12). The *amount* of each nutrient oxidized is computed, with the aid of appropriate factors, from the CO_2 production, O_2 consumption and urinary nitrogen excretion. The heat dissipated by the animal, measured by direct calorimetry, is compared to the computed heat production of the nutrients oxidized. (The heat equivalents of nutrients and their end products are listed in the summary to this chapter.) The observed and computed heat production agreeing to within 1 per cent is taken as proof of the applicability of the first law to animal processes.

2.1.2: The second law.[8] The first law states that all forms of energy are quantitatively convertible to heat. The second law is concerned with the driving force of reactions, with "chemical affinity", with the losses involved in various reactions, and especially limitations on the conversion of heat into work, that is into energy forms other than heat.

The second law is a statement of the experience that the availability of a given energy form for work is dependent on its tendency to "run down" from its relatively high energy level to the general (lower) level, and that there is a tendency toward equalization of energy levels.

Thus steam can do work not because it is hot, but because it is *hotter* than the environment; compressed air can do work not because it has a high pressure, but because it has a *higher* pressure than the environment, and so on. Heat cannot be employed to do mechanical work if it is equally distributed. Only that fraction of atmospheric heat creates wind (which may run windmills) that is distributed unevenly. The heat in the ocean or earth surface is practically unavailable for work because of its practically even distribution. It may, therefore, be said that the total energy of a system is made up of: (1) "bound", unavailable for work, called *entropy*, and (2) "free", available for work. This is one aspect of the second law.

Another aspect of the second law is that only a part of heat energy is convertible to work. This is because work is orderly, relatively large-scale motion, whereas heat is random, uncontrolled, disorderly molecular motion; and it is not possible to convert disorderly into orderly motion of molecules without loss in kinetic energy (heat) of the molecules. Over a century ago (1824) Carnot formulated the equation indicating the maximum heat energy theoretically convertible into work.

Carnot formulated his efficiency equation for heat utilization in an imaginary limiting-ideal engine—one of those scientific fictions so important in the development of science—an engine that is frictionless, does not lose heat and is completely reversible. Carnot's equation is

[8] The second law, older than the first, was formulated in 1824 by S. N. L. Carnot, a 28 year old French Army engineer. The modern elucidation of the second law, however, is due to mid nineteenth century contributions of Clausius, Gibbs, Helmholtz, Lord Kelvin, van't Hoff and others. For the history, see Lewis and Randall, *loc. cit.* p. 5.

$$w = q \frac{T_1 - T_2}{T_1} \tag{2.2}$$

or in the differential form,

$$dw = q \frac{dT}{T} \tag{2.2a}$$

in which w represents the theoretically maximum work-energy obtainable in the ideal Carnot engine from the heat-energy, q, operating between absolute temperatures T_1 of the boiler and T_2 of the condenser.

Under the usual conditions of about 300° C and 30° C at the boiler and condenser respectively, the ideal Carnot engine converts less than half of the heat, q, into work, w. Ordinary heat engines are, of course, much less efficient.[*] Only when the lower working temperature is absolute zero (−273° C) would the Carnot engine convert all the heat energy into equivalent work energy. This brings out another aspect of the significance of absolute temperature and its zero. The zero on the absolute-temperature scale may be defined by the temperature at which the Carnot engine is 100 per cent efficient. This idea will come up again in connection with the discussion of entropy and the "third law" of thermodynamics, which defines the absolute zero as the temperature at which entropy is zero for solids.

Although living organisms are not heat engines (life processes are not operated by temperature differences, and the heat produced by the body is the end product rather than the motive power of the body processes as it is in a heat engine), the principle that the efficiency of transformation of one energy-form into another is less than 100 per cent, even theoretically, appears to be as generally true for isothermal chemical processes as for heat engines.

As applied to isothermal chemical reactions, the Carnot equation (2.2) is usually written (Helmholtz' free-energy equation)

$$\Delta F = \Delta E - T\Delta S \tag{2.3a}$$

or (Gibbs' free-energy equation)

$$\Delta F = \Delta H - T\Delta S \tag{2.3b}$$

in which, as in equation (2.1), ΔE represents the change in intrinsic or internal energy, and ΔH represents the change in heat content; or more simply, it represents the heat of reaction determined by direct calorimetry or computed indirectly with the aid of Hess' law[†] from published thermochemical data[9] of constituent reactions.

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[*] The efficiency, e, of the Carnot engine as given by eq. (2.2) is $e = \frac{T_2 - T_1}{T_1}$.

[†] Hess' law, formulated in 1840, is that the heat liberated or absorbed in a reaction is independent of the manner in which the reaction takes place. Thus the heat of formation of CO, not determinable directly, may be estimated from the following equation indirectly: $C + O_2 = CO_2 + 94$ Cal; $CO + \frac{1}{2}O_2 = CO_2 + 68$ Cal. Therefore, $C + \frac{1}{2}O_2 = CO + 26$ Cal.

[9] "International Critical Tables", McGraw-Hill Book Co., 1929. Landolt, H. H., and Börnstein, R., "Physikalisch-chemische Tabellen", Berlin, 1923. Lewis and Randall, *loc. cit.*

The symbol ΔF represents the free energy change of the reaction, *i.e.*, the theoretically maximum amount of useful work, analogous to w in Carnot's equation (2.2), obtainable from the ΔH of the process at constant temperature and pressure; and $T\Delta S$ is analogous to the part of the heat in Carnot's equation which is not convertible to work.

The numerical values of the free energies, ΔF, of chemical reactions are extremely useful to students of intermediate metabolism in the animal body, as well as to workers in inorganic, organic, and industrial chemistry for predicting the direction and extent of a chemical reaction. It is a measure of the driving force, of the chemical affinity, of the given reaction. If the standard ΔF has a large negative value (exothermic) the reaction will, when properly catalyzed, take place vigorously and essentially completely; if ΔF has a positive value (endothermic) for a given reaction it will not take place unless supplied with energy from external sources; if ΔF is zero, the system is in equilibrium and no change occurs. Indeed ΔF may be, and preferably is, computed from equilibrium data by the equation

$$\Delta F^0 = -RT \ln K \tag{2.4}$$

in which K is the equilibrium constant of the given reaction, ln its natural logarithm, and F° the free energy in a standard state or at unit activity.

In some reactions ΔF may be determined from electromotive-force measurements:

$$\Delta F = -nFE \tag{2.5}$$

in which n is the number of equivalents of chemical change, F the value of the Faraday, and E the electromotive force of the cell.

The characteristic second-law feature in equation (2.3), however, is the term $T\Delta S$, which represents the amount of energy degraded from the free or high-grade form (equivalent to work) to the bound or low-grade form (equivalent to heat) during the process. It corresponds to the wasted heat or bound energy not convertible to work in Carnot's engine [eq. (2.2)].

This increase in bound energy is made up of two factors: capacity, ΔS, and intensity, T (absolute temperature), just as, for example, the work energy of a quantity of heat, q, in steam operating between temperatures T_1 and T_2 is proportional to $q(T_1 - T_2)$.

The *entropy* change in calories per degree (involving simple heat change) is given, for a reversible path, by the equation*

$$\Delta S = \int_{T_1}^{T_2} dS = \int_{T_1}^{T_2} \frac{dq}{T}$$

---

* When the temperature remains constant, as in fusion, $\Delta S = q/T$, derived directly from the Carnot eq. (2.2). Typical entropy values in E.U. for the standard state: C, 1.3; S, 7.6; H_2, 16; $\frac{1}{2}N_2$, 23; $\frac{1}{2}O_2$, 25.

n which dS is the increase in entropy for an infinitesimal change; dq is the infinitesimal mount of heat absorbed; ΔS is the increase in entropy for a finite process. When the emperature is constant (as in fusion), $\Delta S = q/T$.

The numerical value of ΔS of a reaction may be computed from equation (2.3) or, referably independently, from data on heat capacity and latent heat for a wide range f temperature and, in accordance with the third law, extrapolated to absolute zero and he entropy interpolated at the desired temperature. The equation form used for this purpose is

$$S_T' = \Delta\, S_{(0,T)} = \sum_0^T \frac{C_p}{T}\, dT + \sum \frac{\Delta H_{\text{tr}}}{T_{\text{tr}}} \qquad (2.6)$$

n which S_T is the entropy at the absolute temperature T, C_p is the specific (molal) heat* at constant pressure, and ΔH_{tr} is the heat of transition (fusion, etc.), or change in heat content of the substance during the transitions which it undergoes in raising its temperature from the absolute zero, 0, to the given absolute temperature, T. As previously indicated, the "third law" provides a measure of absolute entropy by stating that the term S_0, the entropy at the absolute zero, is equal to zero for systems in equilibrium.

The value of ΔS of a substance may be computed in some cases with the aid of statistical mechanics from spectroscopic data.

The following are illustrative values[10] of ΔH, ΔF, and ΔS at the specified "standard state" or "reference state" of temperature and pressure, in which case the free energy is designated by ΔF°. Unless otherwise specified the "standard state" is assumed to be 25°C (298°K), one atmosphere pressure, and in case of solution one mol per 1000 gm solvent. Each of these conditions, as well as those fixed by these conditions, such as ionization, hydration, solution, etc., affects the thermodynamic values. By way of illustration, consider the oxidation of glucose.

$$C_6H_{12}O_6 + 6O_2 = 6CO_2 + 6H_2O \qquad (2.7a)$$

Since the change of H_2O liquid (l) to H_2O gas (g) involves an energy change

$$H_2O\ (l) = H_2O\ (g) - 9.7 \text{ Cal (at } 100^\circ\text{C)}$$

it is obvious that the value of ΔH in equation (2.7a) will depend on whether the H_2O is in the l or g state. At 25°C and one atmosphere pressure, when the H_2O is in the l state, CO_2 in the g state and $C_6H_{12}O_6$ in the s (solid) state, equation (2.7a) is written:

$$C_6H_{12}O_6\ (s) + 6O_2\ (g) = 6CO_2\ (g) + 6H_2O\ (l) + 674 \text{ Cal} \qquad (2.7b)$$

That is, $\Delta H = -674$ Cal/mol glucose. (The value of $\Delta F^\circ = -685$ Cal). If the H_2O s in the g state, the value of ΔH would be less by $6 \times 10.4 = 63$ Cal than that given in quation (2.7b). According to Baas-Becking and Parks, the free energy of the reaction nder natural conditions when the partial pressure of CO_2 is 0.003 atmosphere is 709 Cal:

$$6CO_2\ (0.0003 \text{ atm}) + 6H_2O \text{ (liquid)} = 6O_2\ (0.2 \text{ atm}) + C_6H_{12}O_6;\ \Delta F_{298} = 708.9 \text{ Cal} \qquad (2.7c)$$

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* Typical heat capacity at constant pressure, C_p per mol: for $H_2 = 6.5 + 0.0009T$; for O_2 and $N_2 = 6.5 + 0.001\ T$.

[10] Taken from Lewis and Randall, *loc. cit.*; Parks, G. S., and Huffman, H. M., "The Free Energies of Some Organic Compounds", New York, 1932; Borsook, H., "Reversible enzymatic reactions", *Ergeb. d. Enzymforschung*, **4**, 1 (1935); Burk, D., "The free energy of nitrogen fixation by living organisms", *J. Gen. Physiol.*, **10**, 559 (1927); *Proc. Roy. Soc.*, **104B**, 153 (1929); *J. Phys. Chem.*, **35**, 432 (1931); Baas-Becking, L. G. M., and Parks, G. S., "Energy relations in the metabolism of autotropic bacteria", *Physiol. Rev.*, **7**, 85 (1927); Needham, D. M., "Energy-yielding reactions in muscle contractions", *Enzymologia*, **5**, 158 (1938). Stephenson, M., "Bacterial metabolism", Longmans, 1939

Likewise as regards pressure. In equation (2.7b) it is assumed to be one atmosphere. Under natural conditions of photosynthesis the partial pressures of CO_2 and O_2 are 0.0003 and 0.2 atmosphere, respectively, and $\Delta F = 708$ Cal rather than 685.

The most interesting biological examples illustrating thermodynamic equations are found in the literature[11] on the metabolic activities of nitrogen-fixing soil bacteria and, of course, in the recent studies on intermediary metabolism in animals.

Most bacteria are *heterotrophs*; they obtain energy for their metabolic processes by oxidation of carbohydrates [eq. (2.7)] and related organic compounds, as does man. But there are, especially among soil bacteria, many *autotrophs*[12] obtaining energy not from oxidation of organic matter but from oxidation of H_2, N_2, S, NH_3, NO_2, Fe^{++}, and so on, as illustrated by the following reactions.

$$C + O_2 = CO_2 + 94 \text{ Cal}$$

$$H_2 + \tfrac{1}{2}O_2 = H_2O + 68 \text{ Cal}$$

$$(\Delta H = -68 \text{ Cal/mol } H_2;\ \Delta F^\circ = -56 \text{ Cal})$$

$$S + 1\tfrac{1}{2}O_2 + H_2O = H_2SO_4 + 142 \text{ Cal}$$

$$(\Delta H = -142;\ \Delta F^\circ = -119)$$

$$S + O_2 = SO_2 + 71 \text{ Cal}$$

The *nitrosomonas* or nitrite producers obtain energy by oxidation of ammonia to nitrites:

$$NH_3 + 1\tfrac{1}{2}O_2 = HNO_2 + H_2O + 79 \text{ Cal}$$

The *nitrobacter* or nitrate producers obtain energy by oxidizing nitrites to nitrates:

$$HNO_2 + \tfrac{1}{2}O_2 = HNO_3 + 21 \text{ Cal}$$

The above are exothermic reactions. The formation of ammonia from atmospheric nitrogen is endothermic.

$$\tfrac{1}{2}N_2 + 3/2\ H_2O = NH_3 + 3/4\ O_2 - 82 \text{ Cal}$$

$$\Delta H = +82 \text{ Cal};\ \Delta F^\circ = +79 \text{ Cal}$$

The energy for the endothermic formation of NH_3 is obtained from the exothermic oxidation of such carbohydrates as glucose which yield 700 Cal free energy per mol, more or less depending on conditions [eq. (2.7b)]. Theoretically, therefore, one mol glucose furnishes sufficient free energy, ΔF, to convert about 4 mols N_2 to NH_3. Actually, however, not one but 30 to 50 mols glucose are required to furnish the needed energy, the "machine efficiency"[11] of the process is only 2 to 3 per cent.

Practically, therefore, the value of ΔF is no better indicator of the "machine" efficiency of a reaction than is the value of w in the Carnot equation (2.2). Living organisms, like engines, have irreversible heat losses due to various causes which in organisms go under the name of "maintenance", and these "maintenance" losses, therefore, tend to be inversely proportional to the speed of the process. There is a time element affecting the irreversible losses.

The value of ΔF, as previously explained, is the best measure of the chemical affinity, the driving force of spontaneous reactions.

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[11] Burk, D., *J. Gen. Physiol.*, **10**, 559 (1927); *Proc. Intern. Cong. Soil Sci.*, **3**, 67 (1930); Baas Becking and Parks, *loc. cit.*

[12] Winogradsky, S., *Ann. Inst. Pasteur*, **4**, 213, 257, 760 (1890); *Id.*, **5**, 92, 577 (1891).

As a matter of fact, however, reactions in biologic systems are not "spontaneous" in the sense that this expression is used in relation to inanimate systems. Biological reactions are mostly *coupled*[13]. Even the conversion of sugar to alcohol and carbon dioxide may be considered as a coupled reaction. The part of the molecule which is oxidized to CO_2 (exergonic[14]) is coupled with and furnishes energy to the part converted to fatty acid or alcohol (endergonic[14]).

$$C_6H_{12}O_6 = 2C_2H_5OH + 2CO_2 + 22\ \text{Cal}$$

(*e. alcohol*)

The following fermentation or glycolysis reactions may also be considered as examples of *internal oxidation-reductions* not involving external (molecular) oxygen:

$$C_6H_{12}O_6 = 2CH_3{\cdot}CHOH{\cdot}COOH + 26\ \text{Cal}$$

(*lactic acid*)

$$C_6H_{10}O_5 + H_2O = 2CH_3{\cdot}CHOH{\cdot}COOH + 32\ \text{Cal}$$

(*glycogen*)

$$(C_6H_{11}O_5 + H_2O = C_6H_{12}O_6 + 6\ \text{Cal})$$

$$C_6H_{12}O_6 = 3CH_3{\cdot}COOH + 15\ \text{Cal}$$

(*acetic acid*)

The fermentation of glucose to produce lactic acid (glycolysis) is an important method of supplying energy to animal tissues when the oxygen supply for normal oxidation energy is inadequate as in violent exercise and in cardiorespiratory insufficiency due to disease. It is, therefore, of great importance in intermediary metabolism. Microorganisms produce in their metabolism a great variety of incompletely oxidized products, a few of which are listed below. Many of them, such as alcohol, acetic acid, citric acid, oxalic acid, kojic acid, gluconic acid, fumaric acid, and so on, are of very great importance.

$$C_6H_{12}O_6 + 4\tfrac{1}{2}O_2 = 3(COOH)_2 + 3H_2O + 493\ \text{Cal}$$

(*oxalic acid*)

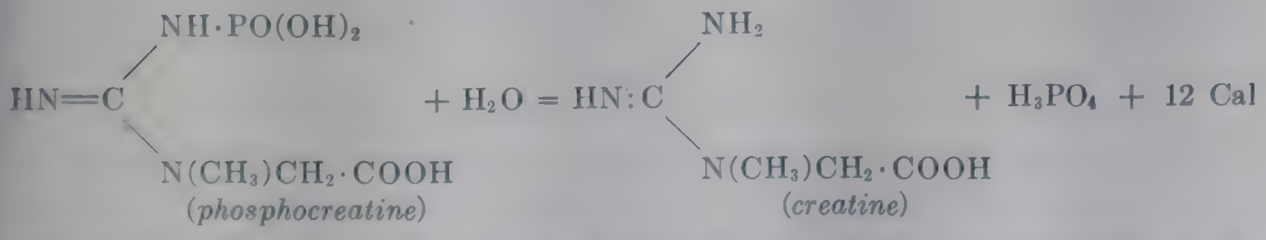
$$CH_3{\cdot}CHOH{\cdot}COOH + KNO_3 = CH_3{\cdot}CO{\cdot}COOH + H_2O + KNO_2 + 31\ \text{Cal}$$

(*lactic acid*) (*pyruvic acid*)

$$CH_3{\cdot}CO{\cdot}COOH + H_2O = CH_3{\cdot}COOH + H{\cdot}COOH + 6.5\ \text{Cal}$$

$$2CH_3{\cdot}CHO + H_2O = C_2H_5OH + CH_3{\cdot}COOH + 22\ \text{Cal}$$

(*acetaldehyde*)



(Phosphocreatine hydrolyzes during muscle contraction and resynthesizes during recovery.)

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[13] *Cf.* Borsook[10], Burk[10], Kolekar, H. M., "The nature of energetic coupling in biological syntheses", *Chem. Rev.*, **28**, 71 (1941).

[14] Coryell, C. D., [*Science*, **92**, 380 (1940)] suggested that the terms *exothermic* and *endothermic* be confined to heat changes, ΔH; exergonic and endergonic be used for designating ΔF changes (*ergon*, from Greek, meaning work).

It should perhaps be re-emphasized in conclusion that we have not been concerned with the internal energy, E, of systems but merely with heat-content *changes*, ΔH; free-energy *changes*, ΔF; and entropy *changes*, ΔS. Thus ΔH, the *heat of formation* of CO from C and O_2 or the *heat of combustion* of C to CO (under standard conditions) is −26 Cal; likewise, the heat of formation of CO_2 from CO, or the heat of combustion of CO to CO_2, is −68 Cal. We are concerned not with total energy but with changes or increments for well-defined reaction stages under well-defined conditions.

Similarly the molal *heat of formation*, ΔH (at 25°C and 1 atmosphere pressure) of formic acid from its elements, C, H_2, and O_2, is −100 Cal and corresponding free energy, ΔF, is −85 Cal; the *heat of combustion*, ΔH, of formic acid to H_2O and CO_2 is −63 Cal, and so on for other compounds as given in the literature.

Another factor needing re-emphasis is that environmental conditions such as temperature, pressure, but *especially concentration* of reactants and products, influence to a greater extent the free energy, ΔF, that is the theoretically maximum work derivable from the energy, than they do the heat-content change, ΔH. The application of this observation is of the greatest practical agricultural importance, especially as it relates to plane of nutrition, which we shall discuss throughout the book. The simple illustration was already cited that in the reaction

$$C + O_2 = CO_2$$

the values of both ΔH and ΔF are −94 Cal per mol when the oxidation is done under a pressure of one atmosphere O_2 and CO_2. But when the partial pressure of CO_2 is 0.0003 atmosphere and of O_2 0.2 atmosphere, the value of $\Delta F = -99$ Cal, whereas ΔH is still −94 Cal.

Finally, an important but apparently mysterious equation needs to be clarified. It was already noted that the work, w, by an expanding gas from volume v_1 to v_2 against a pressure, p, is proportional to $p(v_2 - v_1)$:

$$w \propto p(v_2 - v_1)$$

This proportionality is generalized (when p has always its equilibrium value $\frac{RT}{V}$) to the less evident* equality

$$w = -RT \ln (v_1/v_2) \tag{2.8}$$

in which R is the gas constant (1.988 gm-cal or 0.082 lit-atm) and ln is the natural logarithm (2.303 times the common logarithm) of the given ratio.

Likewise, it may be shown that the free-energy, ΔF, accompanying the dilution of a solution from concentration c_1 to c_2 isothermally is given by the second-law equation form

$$\Delta F = -RT \ln c_1/c_2 \tag{2.8a}$$

This equation form is used for computing kidney work in concentrating urine against a higher osmotic pressure, for electromotive force developed between different ionic concentration, c_1 and c_2, and so on. The free-energy change, $-\Delta F$, equivalent to the work of concentration of urine from blood by the kidney is given[15] by the equation

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* The derivation: $\int_{v_1}^{v_2} p\,dv = \int_{v_1}^{v_2} RT/v\,dv = RT \int_{v_1}^{v_2} dv/v = RT \int_{v_1}^{v_2} (\ln v_2 - \ln v_1) = -RT \ln v_1/v_2$.

[15] For numerical illustration see Borsook, H., and Winegarden, H. M., *Proc. Nat. Acad. Sci.*, **17**, 3 (1931).

$-\Delta F = nRT \ln \frac{\text{C plasma}}{\text{C urine}}$ in which n is the molar concentration in the urine excreted during a given interval. Similarly the work of transporting water from plasma to urine is $-\Delta F = nRT \ln \frac{\text{n plasma}}{\text{n urine}}$.

Turning to more general considerations, the meaning of the definition of the second law, that the difference in energy potentials tend to come to a dead level, is exemplified by daily experiences: when bodies of different temperatures are brought together, the temperatures become equal, thermodynamic equilibrium is established, and the energy becomes useless for work performance.

Statistically viewed, when molecules moving at different speeds (that is, when the bodies are at different temperatures) are brought together, they collide in accordance with the theory of probability, and a compensation of velocities, or thermal equilibrium, is established. Considered in this way, entropy is a condition of maximum probability (Boltzmann). It is improbable that heat will be transferred from a colder to a warmer body, just as it is improbable for a river to rise above its source. Both thermodynamic laws are common-sense laws, with many analogies and implications, yet not without apparent contradictions, two of which may be noted.

The definition of entropy as condition of maximum probability, maximum energetic levelling, maximum disorganization, and so on, all imply a "running down of the universe", an implication which raises the following question often asked by children to whom this concept is explained: if the universe is running down, it must have been previously "wound up". Who wound it up? How was it wound up? What was the "first cause" and the cause of this cause of this winding up?

A second apparent contradiction concerns the evolution of complex organisms from simple and the growth and development of complex bodies from apparently simple eggs (Ch. 16). While there is a tendency toward levelling, yet there are many integrative, directive, creative and individuative activities illustrated by evolution of species, growth and development of individuals, or even by the writing of an orderly book from disorderly data and thoughts.

The fact is that we are not aware of all the factors operating at the living organizational level which may, conceivably, have selective mechanisms analogous on the molecular level to "Maxwell's demon". Probability predictions (Boltzmann derived the second law on statistical considerations) are known to be upset by "thought" (leading to action) with which the living are endowed.

This apparent contradiction may, perhaps, be rationalized, in harmony with Boltzmann's statistical derivation of the second law, by saying that biologic phenomena are relatively local and that general statistical laws need not apply to local events. The limitation of the second law has no significance for single molecular events. Intelligent purposive action may interfere with the normal operation of probability. Thus life insurance tables for the United States do not necessarily reflect the life expectation in a local community living up to unusually high health standards, especially for its children. Improbable events may occur locally in accordance with the calculus of probability and, of course, by proper coupling with external energy-yielding systems. It was noted[16] that biologic syntheses, for example, are normally coupled between two reactions, one representing an increase in free energy, $+ \Delta F_1$, the other a decrease, $- \Delta F_2$, and that the absolute value of ΔF_2 is larger than of ΔF_1. This way one system is more highly organized (entropy lowered) at the expense of simultaneous disorganization (entropy raised) in an interrelated system. In the more familiar example of refrigerating machines heat is raised from a colder to a hotter body; but, of course, by performing work on the system at the expense of external energy. The overall result of such operation is a net increase in entropy, a decrease in free energy. There is philosophic questioning concerning the applicability of the second law to living systems[17], but, as illustrated by the following examples, there is no reason for practical questioning from the standpoint of the present book.

It is sometimes said, and with truth, that the agricultural industry is the only one (with the exception of those utilizing water and wind power) engaged in increasing the supply of free energy for man's use with the aid of green plants, the "great anabolizers", by the basic photosynthetic process

$$6CO_2 \text{ (0.0003 atm)} + 6H_2O \text{ (1)} + \underset{\textit{(solar energy)}}{709 \text{ Cal}} \rightarrow O_2 \text{ (0.2 atm)} + C_6H_{12}O_6 \tag{2.9a}$$

thus supplying the chemical energy for the basic catabolic process

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + 674 \text{ Cal} \tag{2.9b}$$

This photosynthetic process involves a local increase in free energy, a local decrease in entropy. But from the viewpoint of the system as a whole, this geobiologic increase in free energy is coupled or linked with the solar decrease in free energy, and the thermodynamic efficiency of photosynthesis is not very high even theoretically.[18, 19] There is an increase in entropy of the system as a whole; the law of degradation of energy definitely holds. Organisms, however, capture and transform much of the energy that would otherwise be lost.

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[16] *Cf., inter alia*, Ostwald, Wilhelm, *Z. physik. Chem.*, **34,** 248 (1900); Borsook, *loc. cit.;* Kolckar, *loc. cit.;* Burk, D., J., *Physical Chem.*, **35,** 432 (1931).

[17] *Cf. inter alia*, Guye, C. E., "Physico-Chemical Evolution", London, 1925. Jeans, J. H., "Activities of life and the second law of thermodynamics", *Nature*, **133,** 174 (1934); Donnan, F. G., Concerning the applicability of thermodynamics to the phenomena of life. *J. Gen. Physiol.*, **8,** 685 (1926); *Nature*, **133,** 99, 530 (1934); *Scientia*, **24,** 282 (1918). Smuts, J. C., "Holism and Evolution", New York, 1926. Watson, D. L., "Entropy and Organization", *Science*, **72,** 220 (1930).

[18] Borsook[10], p. 39.

[19] *Cf.* Transeau, E. N., "The accumulation of energy in plants", *Ohio J. Sci.*, **26,** 1 (1926): The earth receives about one two billionth of the sun's energy. Of this part received, about 35 per cent is reflected into space, 65 per cent absorbed. Of this absorbed part, 0.12 per cent enters into the life cycle. Of this 0.12 per cent, about 24 per cent is utilized by agricultural plants. Of the 24 per cent utilized by agricultural plants, the plant stores 1 to 25 per cent, some 75 per cent of the energy utilized by the plants being

It may similarly be said that farm animals are wasteful converters of feed into milk, eggs, meat. Thus man obtains about 1500 Cal of useful energy by consuming a pound of grain directly but only about 300 Cal (20 per cent) by consuming milk produced at the cost of a pound of grain (Ch. 21), or about 150 Cal (10 per cent) by eating meat (Ch. 3) or eggs (Ch. 23) produced at the cost of a pound of grain. These animals are, however, humanly useful because they utilize feeds which man cannot or does not wish to utilize directly.* Draft animals have an overall energetic efficiency of about 10 per cent, 90 per cent of the free energy being wasted (Ch. 24). The same is true of inanimate machines, humanly useful but energetically wasteful. In brief, while humanly useful, productive processes involve overall free energy losses: the entropy tends toward a maximum, the free energy to a minimum.

In the case of plant growth, the radiant energy of the sun would be lost anyway, so that whatever photosynthetic use is made of this energy by man is a gain, although the utilization of the energy is low; likewise, while farm animals are wasteful in their utilization of roughage energy, yet whatever utilization is made by the animals for productive purposes is total gain to man who cannot himself consume roughage. Loss and gain are thus relative terms depending on the viewpoint.

2.2: Energy units and energetic equivalents. Equivalent quantities of different forms of energy yield equal quantities of heat (first law). All forms of energy may, therefore, be represented in heat units, Calories or British thermal units (Btu), as indicated in the appendix to this chapter.

While living organisms are not heat engines, it is customary to express the energy exchange in heat units because work energy and storage energy in animals are measured by calorimetric methods, in heat units.

The heat units commonly employed are the *small or gram-calorie*, the heat required to raise the temperature of one gram of water 1° C at 15° C; the *large or kilogram-calorie*, the heat required to raise the temperature of one kilogram of water 1° C, written with a capital C; *mega-calorie*, equivalent to 1000 Cal or 1,000,000 cal, which is Armsby's *Therm*. The Btu is the heat

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used for its maintenance. The overall efficiency of the photosynthetic process is thus extremely small, although the thermodynamic efficiency of the photosynthesis may be 80 per cent. Warburg, O., *Z. physikal. Chem.*, **106**, 191 (1923). See also Spoehr, H. H., *J. Ind. Eng. Chem.*, **14**, 1144 (1922). Holsberg, C. L., *Id.*, **6**, 524 (1924); Briggs, G. E., "Energetic efficiency of photosynthesis in green plants", *Proc. Roy. Soc.*, **105B**, 1 (1929). Wurmser, R., *Ann. d. Physiol.*, **1**, 47 (1925). Adams, E. Q., *J. Am. Chem. Soc.*, **48**, 292 (1926).

* It is said [*Brit. Med. J.*, **2**, 269 (Aug. 2, 1941)] that the protein mainstay of the German Army is not meat but "brattling", a soybean skimmilk sausage; that, likewise, peanut and cottonseed meal (after the oil has been extracted therefrom), usually fed to cattle, is at present used in Germany as a meat substitute in the form of sausage, etc., at, perhaps, 10 per cent of the cost of meat." Soybean is, of course, a staple in China.

required to raise the temperature of 1 lb of water 1° F. A Calorie (kg-cal) is thus about 4 Btu (3.9681 Btu) or 1 Btu is equivalent to about $\frac{1}{4}$ Cal (0.2522 Cal).

2.3: Feed and nutrient energy categories. There appears to be some analogy between the thermodynamic energy categories discussed in section 2.1 and the feed and nutrient categories discussed in this section.

Thus the energy equivalent of the oxygen consumed (about 5 Cal/lit) by a working animal above that consumed at rest is analogous to what was called ΔH in section 2.1, the total energy associated with the work, and the maximum theoretically obtainable work by the animal is analogous and, perhaps, close to what was termed free energy, ΔF, in section 2.1.

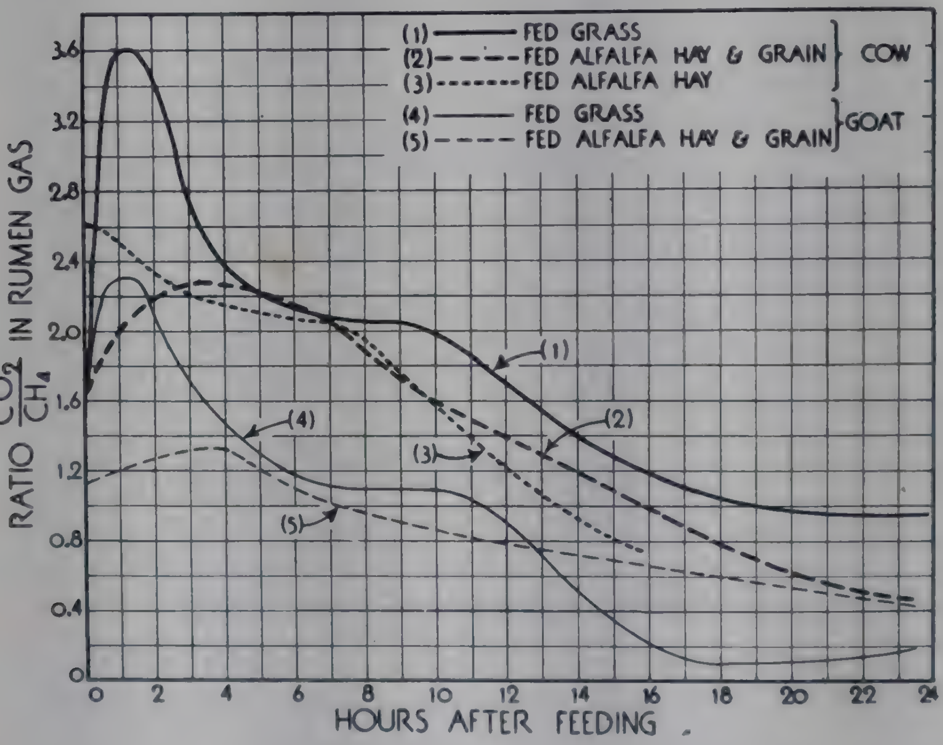

Fig. 2.1—Ratio of CO_2 to CH_4 in the rumen of cattle and goats.[21]

We shall discuss four feed and nutrient categories: *net energy*, sometimes called "production energy", equivalent to Kellner's "starch values"; *metabolizable energy; digestible energy* or TDN; *gross energy.*

The *net-energy* category formulated and defined by Armsby[20] as the maximum proportion of the feed energy convertible to work, milk, egg, meat, and maintenance seems to correspond to the free energy, ΔF, of thermodynamics, although the latter is confined to the theoretically maximum (not actual) energy convertible to work, and not to storage (as for milk production).

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[20] Armsby, H. P., "The Principles of Animal Nutrition", 1903; "The Nutrition of Farm Animals", 1917; "Net Energy Values for Ruminants", Penn. State College Bull. 42, 1916. See also Fraps, G. S., "Practical applications of productive energy values to problems concerning feeds and feeding", *Proc. Am. Soc. Animal Production*, 1937; "The production coefficients of feeds", Texas Agr. Exp. Sta. Bulls. 185 (1916), 203 ('16), 329 ('25), 373 ('28), 402 ('28), 436 ('31), 454 ('32), 461 ('32).

The analogy, here as elsewhere, between nutrient and thermodynamic categories is only formal.

The *metabolizable-energy* (or physiological fuel value) category, defined by Armsby[20] as the net energy plus heat increment of feeding, seems to correspond to change in the heat content, ΔH, of thermodynamics.

The heat increment (above the postabsorptive level) associated with the nutritive process, usually called "specific dynamic action", or SDA—which might be called food-utilization tax—appears to be analogous to the entropy term, $T\Delta S$, of thermodynamics.

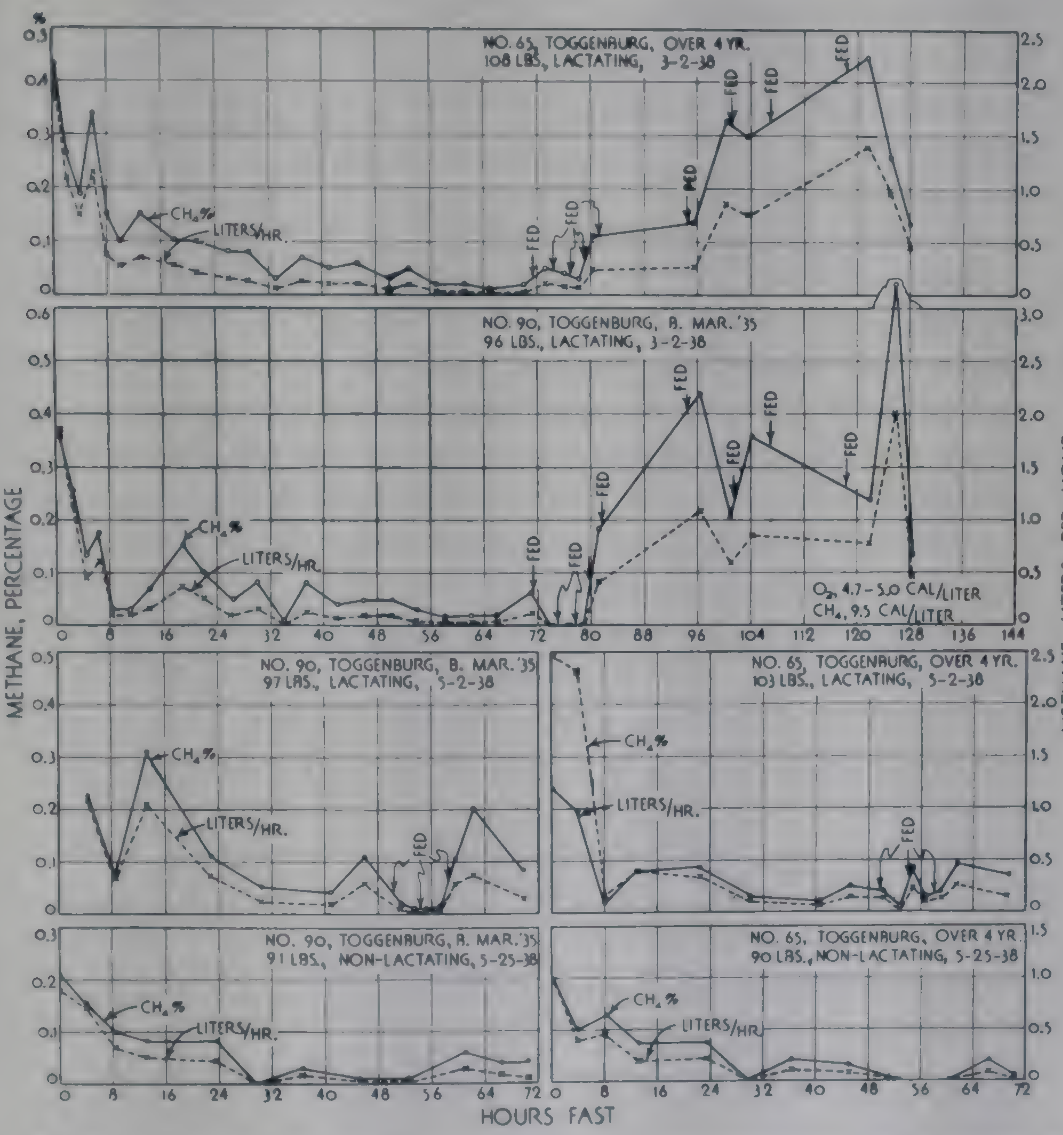

Fig. 2.2—Time curves, following feeding, of methane percentage and methane volume in expired air of goats (see also Fig. 12.8 b, p. 323).

And just as we have the basic thermodynamic equation

$$\Delta F = \Delta H - T\Delta S \tag{2.3}$$

so we may write

$$NE = ME - SDA \tag{2.10}$$

in which NE is the net energy, ME is the metabolizable energy, and SDA the specific dynamic action or the heat increment of feeding. This analogy is closer for work processes than for maintenance and storage, to which the net energy concept also applies.

The other two feed categories are *gross energy*, which is simply the combustion value of the original feed or food; and *digestible energy* which is the gross energy less the fecal energy.

The gross-energy category has no important nutritional significance since it gives no clue to the nutritional value of the feed. Thus the gross energy (combustion value) per unit weight is practically the same for dry starch as for dry wood, despite the fact that starch is utilized completely by the body, whereas the wood is not utilized at all.

While the *digestible-energy* category is much more significant nutritionally than gross energy, it is also ill-defined. The so-called digestible energy, defined by the difference in combustion value of the feed and feces, is not really, but only apparently digestible, since the feces contain not only indigestible material but also voluminous excretions from the body proper into the digestive tract and secretions of juices and enzymes by the digestive-tract wall, as well as abrasions from the walls and a rich flora of bacteria and, in cattle especially, a fauna of protozoa. The *metabolic* part of the feces (not part of the undigestible feed or food) is highly variable depending on the amount of roughage in the ration, plane of nutrition, balance between nutrients and so on.

Moreover, some species, such as ruminants, produce anaerobically (by fermentation) enormous quantities of gases which have a high caloric value. These gases, not being part of the feces, are consequently classed with the digestible nutrients!

The most voluminous gases in the rumen are[21] CH_4 and CO_2, but there are also said[22] to be H_2, H_2S, and CO (Fig. 2.4). Fatty acids are also formed.[21]

It is difficult to determine the ratio of CO_2 to CH_4 because the fatty acids formed in fermentation liberate CO_2 from carbonates. We obtained data on the CO_2/CH_4 ratios *as they exist* in the paunch of cattle, goats, and sheep at various times after feeding; as well as percentages of methane in expired air, as shown in Figs. 2.1 and 2.4. These data enabled us to estimate that the average well-fed dairy cow produces about 300 liters per 24 hours of each fermentation product,[23] CH_4 (Fig. 2.4) and CO_2. Assuming that the energy equivalent is 9.5 Cal/lit for CH_4 and 4 Cal/lit for CO_2, the fermentation-energy loss is about 4000 Cal/day,[24] equivalent to about a third of the resting maintenance energy cost of a 1200-lb cow (Ch. 15).

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[21] Washburn, L. E., and Brody, S., "Methane, hydrogen, and carbon dioxide production in the digestive tract of ruminants", Univ. Missouri Agr. Exp. Sta. Res. Bulls. 263, 1937, and 295, 1939.

[22] Olson, T. M., "Ruminant gases", *J. Dairy Sci.*, **25**, 684 (1942).

[23] See, also, Cole, H. H., Mead, S. W., and Kleiber, M., "Bloat in Cattle", Calif. Agr. Exp. Sta. Bull. 662, 1942.

[24] According to Rossini [*J. Research*, **6**, 49 (1931)] the molar heat of combustion of CH_4 at 25°C and one atmosphere is 212.8 Cal.

The fermentative production of fatty acids, methane, and CO_2 in the rumen may be variously represented, as

$$\underset{\text{(cellulose)}}{2C_6H_{10}O_5} \longrightarrow \underset{\text{(butyric acid)}}{2C_4H_8O_2} + 3CO_2 + CH_4$$

after Krogh and Schmit-Jensen[25], involving a 3 to 1 proportion between the volumes of CO_2 and CH_4; or it may be imagined to occur as follows[26]:

$$(1)\ C_6H_{10}O_5 + H_2O \rightarrow 3CO_2 + 3CH_4; \qquad (2)\ CO_2 + 4H_2 \rightarrow CH_4 + 2H_2O$$

The above discussion indicates a great loss of feed energy in the form of fermentation gases. The loss may not, however, be as great as it seems, because the fermentation losses appear to come from the indigestible part of the ration, or the fermentation loss is compensated by greater digestibility associated with the fermentation process. This is indicated by the fact that the percentage of metabolizable energy of a given ration is the same for cattle and rabbits (Figs. 5.3 and 5.4), despite the great difference in fermentation gases produced by these two species.

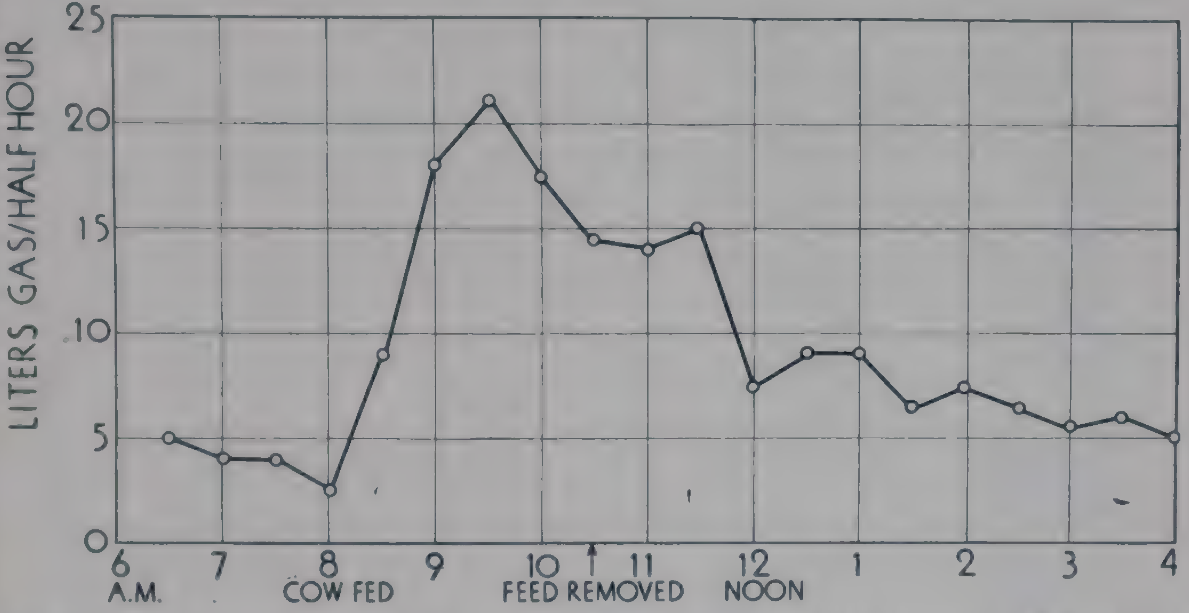

Fig. 2.3—The time course of gas formation after green alfalfa feeding (Cole, *et al.*).[23]

The *metabolizable energy*, or *physiologic* fuel value, category in nutrition (eq. 2.10) corresponds to the heat change, ΔH, in thermodynamics (Section 2.1). The *physiologic* fuel value of nutrients, especially of nitrogenous nutrients, is considerably below that of the *bomb-calorimeter* fuel value, ΔH, because the *oxidizing powers of the body* are below those of the bomb calorimeter. Thus protein is not completely oxidized in the body: for each gram of protein catabolized about 1.3 Cal are excreted in the urine in the form of incompletely oxidized products such as urea, creatinine, and so on, thus reducing the bodily oxidation value of protein to 4.35 Cal/g, or 1973 Cal/lb from the calorimeter-combustion value of about 5.65 Cal/g or 2563 Cal/lb. Less conspicuous urinary energy losses are incurred by other nutrients. Moreover, as previously noted, gas production in the digestive tract involves losses of partly oxidized products. It will be shown in Chapter 5 that the metabolizable-energy category, obtained by deducting these losses from the digestible-energy category, is about 85 per cent of the *TDN* (digestible-energy category) in cattle and about 93 per cent of the *TDN* in rabbits, the exact percentage depending on the plane of nutrition, balance between nutrients, and especially the amount of fermentable material fed.

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[25] Krogh, A., and Schmidt-Jensen, H. O., "The fermentation of cellulose in the paunch of the ox and its significance in metabolism experiments", *Biochem. J.*, **14**, 686 (1920).

[26] Barker, H. A. [*Arch. Mikrobiol.*, **7**, 404, 420 (1936)] reported methane production by bacteria, thus: $CO_2 + 2C_2H_5OH \rightarrow CH_4 + 2CH_3OH$. The alcohol or similar compound acts as the H donor for reducing CO_2.

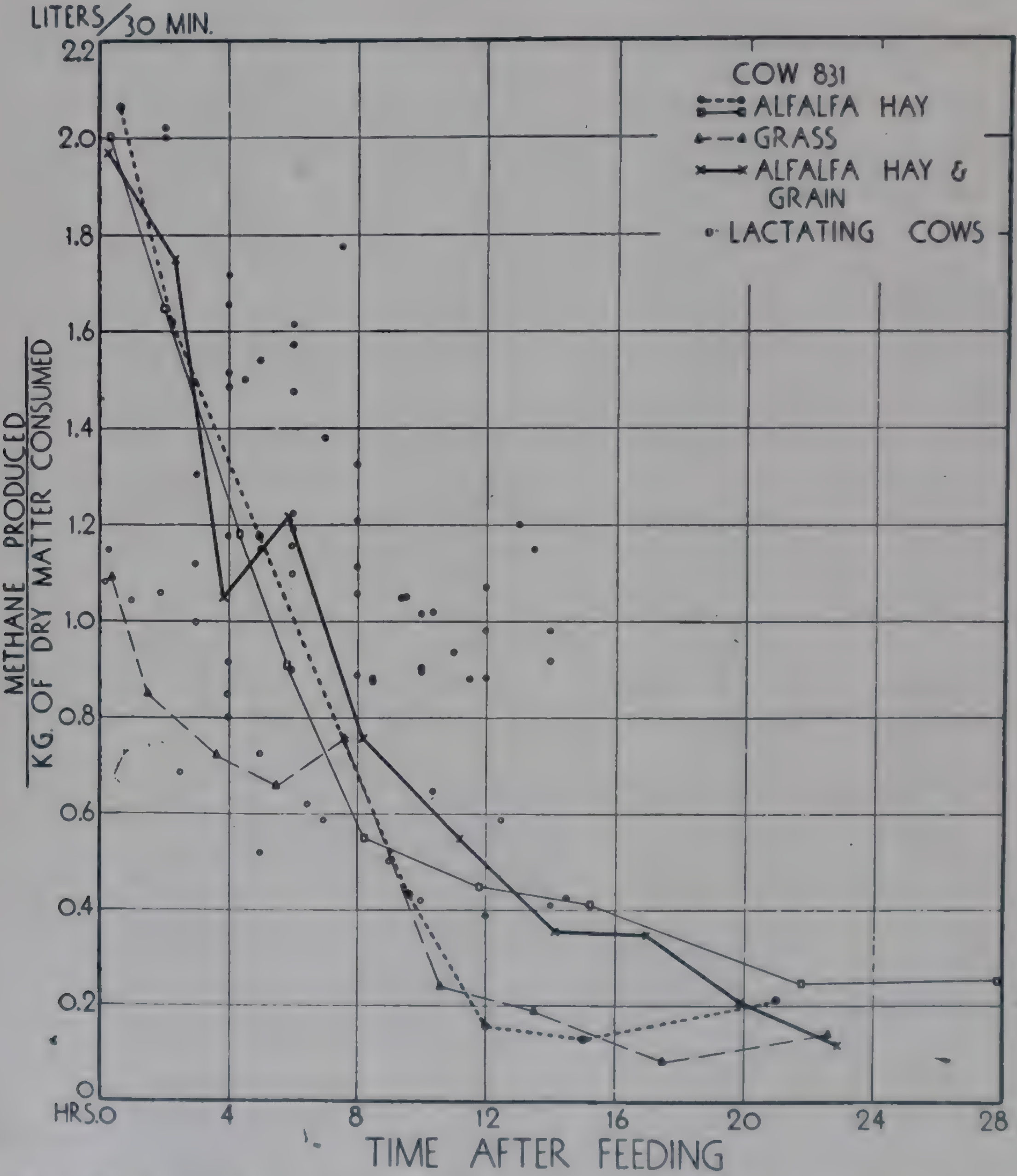

Fig. 2.4a Time course of composition of rumen gas in Jersey cow 831[21] following feedings of alfalfa hay; grass; alfalfa hay and grain.

The *net-energy* category in nutrition corresponds to the free-energy change, ΔF, in thermodynamics. Armsby[27] built his famous cattle-respiration calorimeter for the purpose of measuring this *net-energy* category of nutrients.

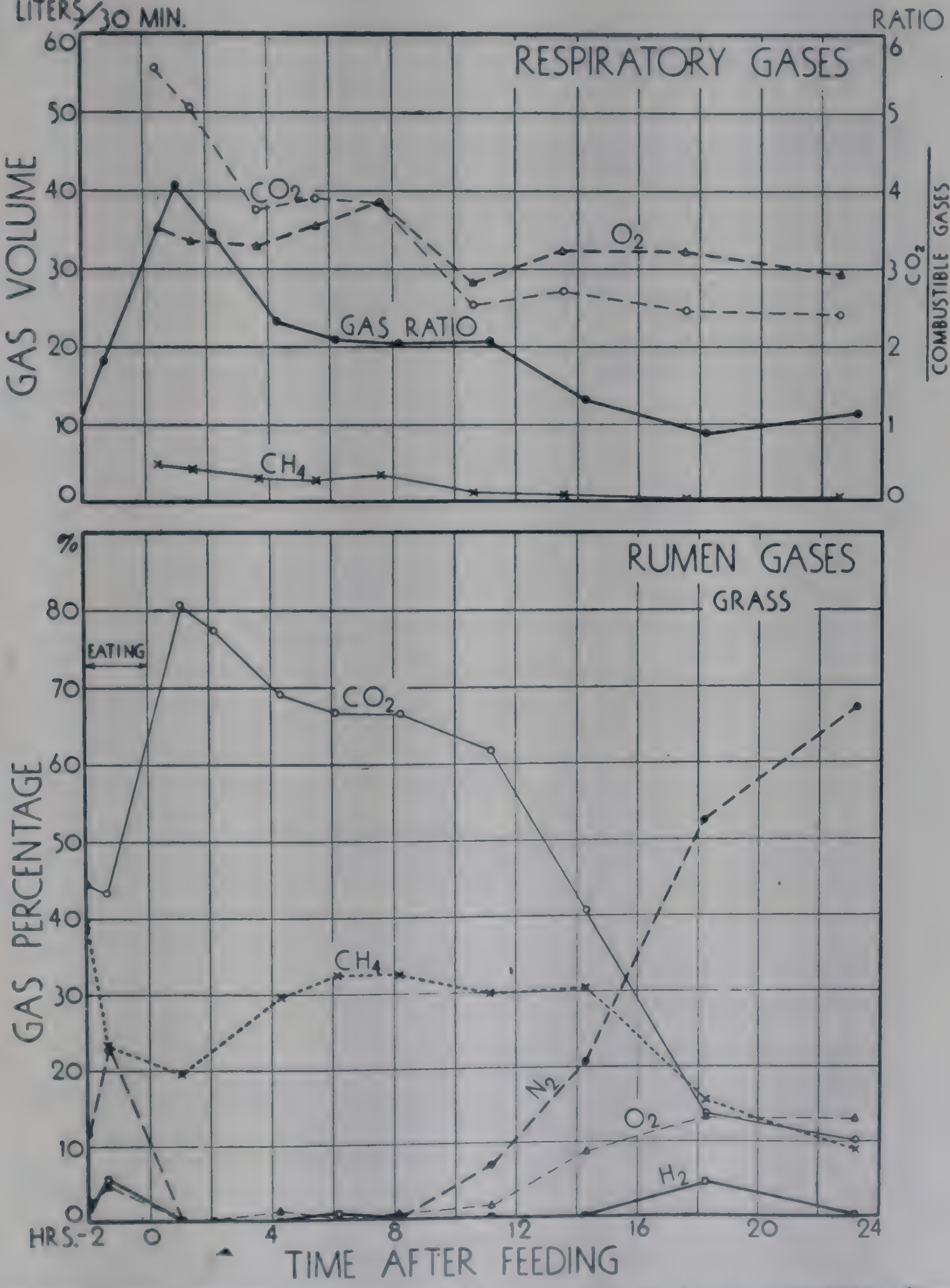

Fig. 2.1b—Time course of composition of rumen gas in Jersey cow 831[21] after feeding of grass.

Unfortunately, it is more difficult to evaluate the net energies of feeds than the free energies of chemical reactions. The net-energy category has not, therefore, come into practical use in the feeding of farm animals. Instead the *digestible-nutrient* category, termed for short *TDN*, is commonly used in the feeding of farm animals.[28]

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[27] Armsby, H. P., "Nutrition of Farm Animals", 1917.

TDN = digestible carbohydrates + digestible protein + digestible fat × 2.25.

The conversion of weight units, such as grams or pounds *TDN*, or metabolizable nutrients, or net-energy nutrients, to Calories offers difficulties. The *average* heats of oxidation of the three principle foodstuffs in a bomb calorimeter are estimated[29] to be

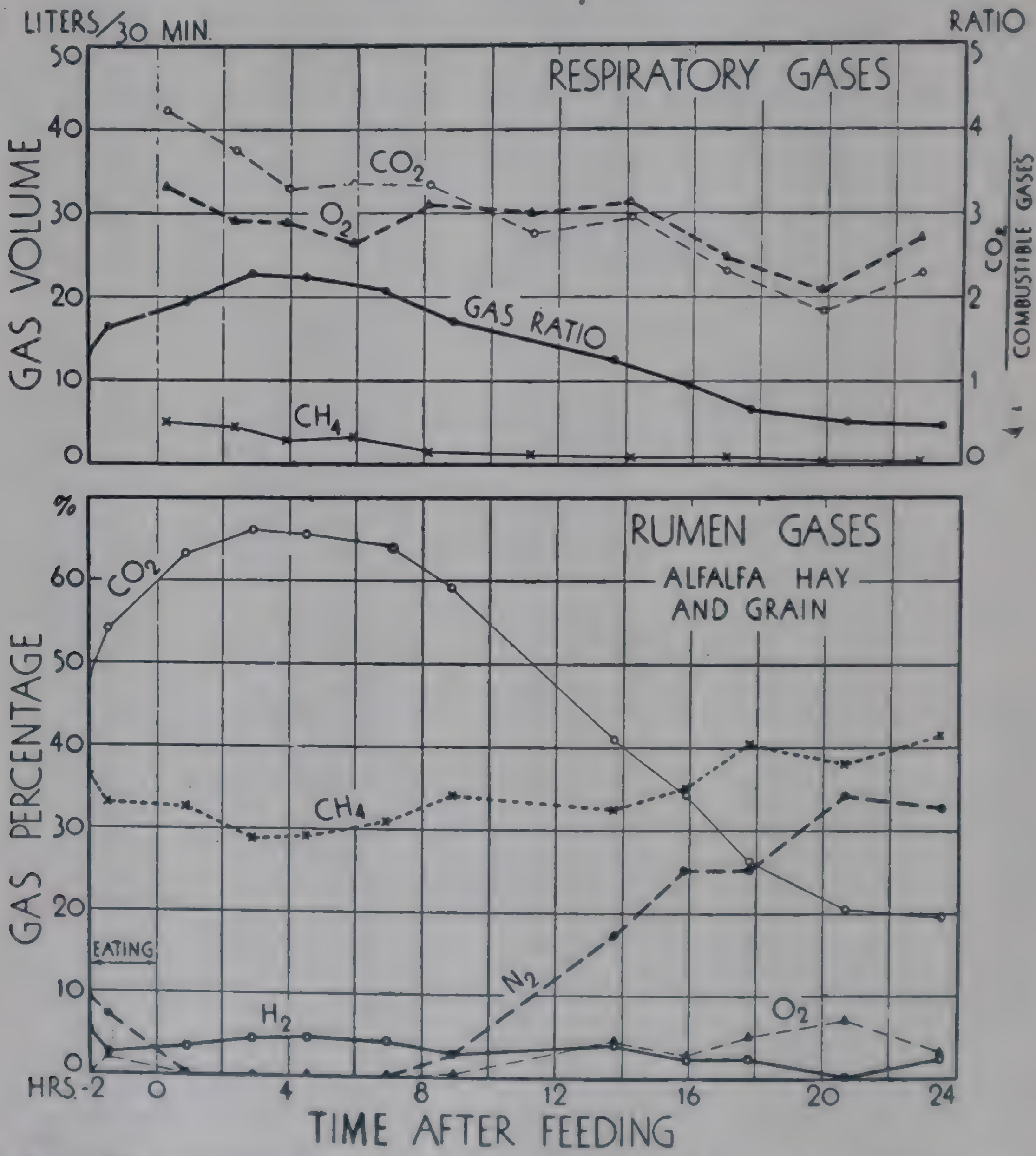

Fig. 2.4c—Time course of composition of rumen gas in Jersey cow 831[21] after a feeding of alfalfa hay and grain.

Carbohydrates	4.10 Cal/g	1860 Cal/lb
Fats	9.45 Cal/g	4287 Cal/lb
Protein	5.65 Cal/g	2563 Cal/lb

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[28] Morrison, F. B., "Feeds and Feeding", 1936, presents extensive *TDN* tables.

[29] Fries, J. A., U. S. Dept. Agr. Bureau of Animal Industry, Bull. 94, 1907. Armsby, *loc. cit.* Atwater, W. O., and Bryant, A. P., "The chemical composition of American food materials", U. S. Dept. Agr. Bull. 28, 1903. Benedict, F. G., and Atwater, W. O.,

It must be emphasized that there are very wide variations in individual determinations.[29]

The convention had developed among students of human nutrition[30] to multiply the grams carbohydrate in the diet by 4, the grams of the protein in the diet by 4, and the grams of fat in the diet by 9, and assume that the result represents the *physiologic* fuel value (metabolizable energy Cal) of the diet. The difference between these 4:4:9 physiologic-fuel factors and 4.10:5.65:9.45 bomb-calorimeter conversion values previously cited is assumed to represent the dietary losses in the urine (energy of creatinine, urea,

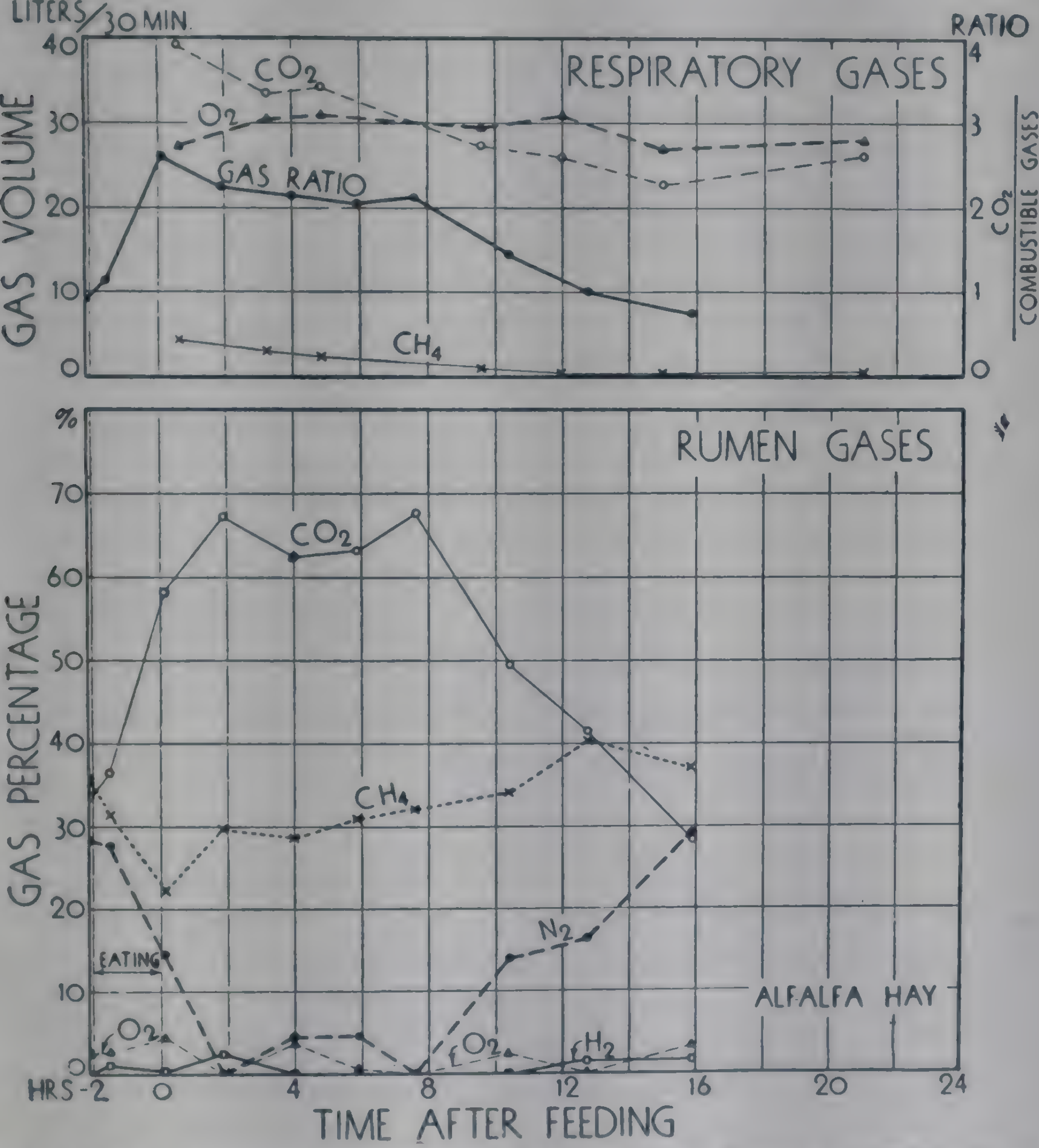

Fig. 2.4d—Time course of composition of rumen gas in Jersey cow 831[21] after a feeding of alfalfa hay.

Id., Bull 136, 1903. Benedict and Milner, *Id.*, Bull 175, 1907. Rubner, M., "Die Gesetze des Energieverbrauchs bei der Ernahurng", 1902. Sherman, H. C., "Chemistry of Food and Nutrition", Macmillan, 1938. Landolt and Bornstein, *loc. cit.* "International Critical Tables", *loc. cit.* Maynard, L. A., "Animal Nutrition", 1937.

[30] Sherman, H. C., *loc. cit.*; Chatfield, C., and Adams, G., "Compilation of American food materials". U. S. Dept. Agr. Circular 549, 1940.

etc., amounting to about 1.3 Cal/g protein), feces (assumed 2 per cent loss for carbohydrates, 5 per cent loss for fats and 8 per cent loss for proteins), and fermentation gases.

There is no agreement for the conversion of animal feeds to metabolizable energy. Some authors estimate the metabolizable-energy values in ruminants by assuming that they produce 4.5 g CH_4 per 100 g digested carbohydrate, and that this CH_4 together with the associated CO_2 has a thermal equivalent of 60 Cal per 100 g, or 273 Cal per lb, of digested carbohydrate[31]; and that the urinary energy in cattle is between 4 to 5 per cent of the gross feed energy (Ch. 5). Armsby[32] reported (for cattle) metabolizable values of 1600 Cal (1500–1700) per pound *TDN* for roughages, 1830 Cal (1720–2200) for concentrates, and 1660 Cal (1580–1870) for mixed rations. Christensen and Hopper[33] reported (for sheep) 1670 Cal for roughages and 1690 Cal for mixed rations. Forbes and Kriss[34] reported 1690 Cal metabolizable energy per pound *TDN*, or about 3.6 Cal per g *TDN*. In the interest of uniformity the writer suggested[35] that the *TDN* be converted to Calories by multiplying g *TDN* by 4, or lbs *TDN* by 1814, or oz *TDN* by 113.4. The resulting caloric values would represent, roughly, the metabolizable energy of the *TDN*. The conversion factor 4 Cal/g *TDN* is somewhat too high for ruminants and somewhat too low for omnivors and carnivors. In any case, the given conversion factor is a rough estimate, and its relation to the actual metabolizable energy necessarily depends on the nature of the ration and in ruminants on the amounts of rumen fermentation. To avoid complications with consequent misunderstandings, we say that our efficiency-computations in this book will be based in most cases with respect to consumed *TDN*, assuming that 1 g *TDN* is equivalent to 4 Cal or 1 lb *TDN* to 1814 Cal.

The above considerations make it evident that the apparent efficiency of a biologic process, as defined by equation (1) (Ch. 1) depends on the nutrient category used as reference base [denominator in eq. (1)]. The apparent efficiency is greatest when employing the net-energy category in the denominator as reference base, and least when employing the gross-energy category. For muscular work, the efficiency with respect to the *net-energy* category is represented by the rate of oxygen consumption of work above rest, thus:

$$\text{Net efficiency of work} = \frac{\text{work accomplished in Cal. equivalents}}{\text{oxygen consumed at work above rest in Cal. equivalents}}$$

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[31] Kellner, [*Landw. Vers.-Stat.*, **53**, 415 (1900)] reported 4.2 to 4.3 g CH_4 per 100 g carbohydrates digested. Armsby ("Nutrition of Farm Animals", p. 638) reported 4.8 g CH_4 for roughages and 4.7 g for concentrates.

[32] Armsby, H. P., "The Nutrition of Farm Animals", p. 278. See also Penn. State College Bull. 42, 1916, on "Net Energy for Ruminants".

[33] Christensen, F. W. and Hopper, T. H., "Digestible nutrients and metabolizable energy in certain silages, hays, and mixed rations", *J. Agr. Res.*, **57**, 477 (1938).

[34] Forbes, E. B., and Kriss, M., *Proc. Soc. Animal Production*, p. 1131 (1931).

[35] Brody, S., "Report of the conference on energy metabolism", National Research Council, Washington, 1935.

If the Calorie equivalent of oxygen consumed is replaced by the Calorie equivalent of the total feed consumed, the apparent efficiency will be only 50 per cent of that when oxygen is used as reference base, since the net energy of herbivor's feed is about 50 per cent of the gross energy.

2.4: Summary and appendix. Section 2.1 discusses the principles of thermodynamics and their relation to biology and especially to agriculture. The thermodynamic uniqueness of the agricultural industry is that it increases the local available free energy (or decreases the entropy) for man's use by utilizing the solar radiant energy which would otherwise be lost. It appears that, with one or two exceptions, all other human activities lower the local free-energy[36] reservoir. This explains the national importance of agriculture in general and of soil conservation in particular, since soil is the basic national resource, the thread that binds us, by way of plants, to the source of all energy, the sun.

Some attention is given to the philosophic aspects of the applicability of the principle of degradation of energy to such constructive processes as growth, development and evolution of organisms. An attempt was made to bring out formal analogies between nutrient and thermodynamic categories.

The following symbols and definitions were used in Section 2.1.

ΔE: Change in internal energy of a system during a process. ΔU is often employed synonomously with ΔE.

ΔH: Change in heat content associated with a process, as in the heat of combustion or heat of formation. This includes pressure-volume energy as indicated by the relation $\Delta H = \Delta E + \Delta(PV)$ and by $\Delta H = \Delta E + P\Delta V$, in which $\Delta(PV)$ represents change in pressure volume product and $P\Delta V$ is work done by or upon the system.

Carnot Cycle: a theoretical sequence of operations converting heat at a higher temperature, T_1, to work plus heat at a lower temperature, T_2.

ΔS: Change in entropy, in bound energy, in low-grade energy, in randomness, **not** convertible to work.

ΔF: Change in free energy, which is capacity to do work or in the theoretically obtainable maximal useful work from the reaction at constant pressure and temperature. $\Delta F = \Delta H - T\Delta S$ is the fundamental thermodynamic equation for a process at constant pressure and temperature corresponding to Carnot's equation for a process involving a temperature gradient. (When there is also pressure-volume work, the maximum work including this pressure value is represented by ΔA, and $\Delta F = \Delta A - P\Delta V$.)

T: Absolute temperature = Centigrade temperature, t, +273°.

K°: Absolute temperature scale (named after Lord Kelvin) for which the zero is −273.1°C.

ln: Natural logarithm, 2.3026 times the common logarithm.

e: Base of natural logarithms, 2.71828.

F: Faraday = 96,500 coulombs = 23.07 Cal

q: Heat absorbed [eq. (2.1)].

w: Work done [eq. (2.1)].

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[36] *Cf.* Ostwald, Wilhelm, "Der Energetische Imperative", Leipzig, 1919. The imperative reads, "Waste not free energy, treasure it and make the best use of it". In 1886 Boltzmann expressed the same idea: "The struggle for existence is a struggle for free energy".

R: Gas constant = 1.987 Cal/degree = 8.31507 joules/degree = 8.31507 volt-coulombs.
n: Number of equivalents or mols involved.
C_p: Heat capacity at constant pressure per mol.
C_v: Heat capacity at constant volume per mol.
Q_{O_2}: c.mm. of O_2 taken up per mg dry tissue per hour; Q_{CO_2}: = c.mm CO_2 given out per mg dry tissue per hour.

Section 2.2 discusses the energy units employed in agricultural bioenergetics, especially as they relate to farm animals. It is suggested that the kilogram-calorie, designated by Calorie with a capital C, be employed as the basic unit. Armsby's *Therm*, or mega-calorie, is 1000 Calories. The following conversion table shows several interrelations.

(See following pages for caloric equivalents.)

Section 2.3 discusses the four feed and nutrient energy categories: net energy, metabolizable energy, digestible energy and gross energy, also the heat increment of feeding (*SDA*) and the fermentation, urinary and fecal energy losses.

SDA: "Specific dynamic action", the heat increment of feeding above the post-absorptive level. It is analogous to the entropy term, $T\Delta S$, in thermodynamics.
N.E.: Net energy is the gross energy (combustible energy of the original material) less the fecal, urinary, fermentation-gas, and *SDA* energy. It is the energy convertible into the maximum amount of work, milk, egg, meat, etc. It is analogous to the free energy term, ΔF, in thermodynamics.
M.E.: Metabolizable energy is *N.E.* plus the *SDA*. *N.E.* = *M.E.* − *SDA*. It is the gross energy less the fecal, urinary and fermentation energy. It is analogous to the ΔH term in thermodynamics.
D.E.: Digestible energy is gross energy less fecal energy.
TDN: Total digestible nutrients = digestible carbohydrates + digestible protein + digestible fat × 2.25. 1 g *TDN* is estimated to be roughly equivalent to 4 Cal/g or 1814 Cal/lb. The exact value depends on species, plane of nutrition, balance between nutrients and other factors, and is, therefore, subject to correction and even debate. The average *calorimetric*-combustion values are, however, fairly definite, about 4.1 Cal/g for carbohydrates, 5.6 for protein and 9.4 for fat.

It will be shown in Chapter 5 (Fig. 5.4) that empirical observations on cattle yield the following energy values for the several categories.

	Gross energy of feeds (heat of combustion)		Digestible energy		Metabolizable energy (physiological fuel value)		Net energy of feed	
	(Cal/g)	(Cal/lb)	(Cal/g)	(Cal/lb)	(Cal/g)	(Cal/lb)	(Cal/g)	(Cal/lb)
Cattle	4.5	2000	3.2	1600	2.7	1200	2.2	1000
Rabbit	4.5	2000	2.9	1300	2.7	1200	2.3	1000

Percentage values

	Digestible energy, % of gross	Metabolizable energy, % of		Net energy, % of		
		gross	digestible	gross	digestible	metabolizable
Cattle	71	60	85	49	69	81
Rabbit	64	60	93	51	79	85

In general, the heats of combustion of nutrients vary directly with the hydrogen and carbon content, and inversely with the oxygen content, roughly

Approximate Combustion Values, Cal/g

Carbon	8	Succinic acid [$C_2H_4(COOH)_2$]	3.0
Hydrogen	34.5	Oxalic acid [$(COOH)_2$]	0.668
Sulfur	3.2	Citric acid ($C_6H_8O_7$)	2.478
Methane	13.3	Lactic acid (C_2H_5OCOOH)	3.66
Ethyl alcohol (C_2H_5OH)	7.07	Urea (CH_4ON_2)	2.528
Glycerol [$C_3H_5(OH)_3$]	4.3	Creatinine ($C_4H_2N_3O$)	4.6
Glucose ($C_6H_{12}O_6$)	3.75	Creatine ($C_4H_9O_2N_3$)	4.24
Sucrose ($C_{12}H_{22}O_{11}$)	4.0	Uric acid ($C_5H_4O_3N_4$)	2.74
Lactose ($C_{12}H_{22}O_{11}$)	4.0	Glycin ($C_2H_5O_2N$)	3.11
Starch ($C_6H_{10}O_5$)	4.2	Tyrosin ($C_9H_{11}O_3N$)	5.915
Acetaldehyde (CH_3CHO)	6.12	Alanine ($C_3H_7NO_2$)	4.35
Acetic acid (CH_3COOH)	3.49	Urinary nitrogen substances in rats on casein diet: 3.059 Cal. equivalent to 6.67 lit. O_2 or 5.47 lit CO_2	
Propionic acid (C_2H_5COOH)	4.96		
Butyric acid (C_3H_7COOH)	5.95		
Palmitic acid ($C_{16}H_{32}O_2$)	9.35		
Stearic acid ($C_{17}H_{35}COOH$)	9.53	Wood, sugar, charcoal	8
Oleic acid ($C_{18}H_{34}O_2$)	9.5	Gluten	6
Tributyrin ($C_{15}H_{26}O_6$)	6.4	Hemoglobin	5.9
Olive oil	9.4	Casein	5.7
Hog fat	9.5	Egg yolk	8.1
Sheep fat	9.5	Egg albumin	5.7
Butterfat	9.2	Muscle	5.7

*Heats of Combustion of Nutrients or Feeds**

	Heats of combustion in terms of several commom units					Elemental Composition			
	Cal/g	Cal/kg	Cal/lb	Cal/oz	Therms/ 100 lbs	C %	H %	O %	N %
Starch and glycogen	4.1	4200	1905	119	190.5	44	6.2	49	
Sucrose	4.0	4000	1814	113	181.4	42	6.4	52	
Glucose	3.8	3800	1724	108	172.4	40	6.7	53	
Fat	9.45	9400	4264	266	426.4	75	11.8	13	
Protein	5.65	5700	2585	162	258.5	52	7.0	23	16
Urea	2.5	2500	1134	71	113.4	20	6.7	27	47
Creatinine	4.6	4600	2040	128	204.1	43	6.2	14	37
Corn meal	4.4	4400	2000	125	200				1.4
Straw	4.4	4400	2000	125	200				0.6
Hay	4.5	4500	2040	128	204				1 to 2
Soybeans	5.5	5500	2500	156	250				5.9
Wheat bran	4.5	4500	2040	128	204				2.5
Linseed oil meal	5.1	5100	2313	145	231				5.6
Average cattle and rabbit ration	4.5	4500	2040	128	204				

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* Conversion factors used: 1 kg = 1000 g = 2.205 lbs = 35.274 oz; 1 lb = 16 oz = 453.6 g = 0.4536 kg; 1 oz = 28.35 g. See preceding reference, Sherman, Morrison, Maynard, and others for sources of data.

in proportion to the combustion values of hydrogen, carbon, and oxygen as indicated in the following table. (The heat of combustion of hydrogen in Cals/g is 34.5; carbon 8.08; sulfur, 3.2; methane, 13.35; ethyl alcohol, 7.07; the heat equivalent of oxygen is 2.6 to 3.4 Cal/g or 4.7 to 5.1 Cal/liter). The average heat of combustion of carbon in tissue is assumed to be the same as in glucose, 113 Cal per gram atom of carbon.

The following tables list additional illustrative values of heats of combustion of nutrients, feed stuffs, and several familiar substances and other equivalent values used in this book.

Table of Energetic Equivalents

Metabolic water from nutrients
100 g protein yields 41 g H_2O
100 g fat yields 107 g H_2O
100 g CH yields 60 g H_2O

Heat equivalent of O_2 and CO_2
1 liter O_2 = 5.14 Cal for glycogen
4.4 Cal for oils (cottonseed, cod liver, corn, etc.)
4.6 Cal for fat (as butterfat)
4.6 Cal for protein
5.06 Cal for starch
5.08 Cal for sucrose
4.8 Cal for hay
22.4 lit. O_2 = 30 g glycogen.
1 lit. O_2 = 5 Cal (5.05 at R.Q. 1.0, and 4.69 at R.Q. 0.70, and 4.825 at R.Q. 0.82)
= app. 15,500 ft-lbs (15,580 to 14,470) = 2134 kg-m (2155 to 2001).
1 lit. CO_2 = 5 to 6.7 Cal (5.05 at R.Q. 1.0, and 6.7 at R.Q. 0.70).
1 g CO_2 = 2.5 to 3.4 Cal (2.57 at R.Q. 1.0, and 3.41 at R.Q. 0.70).
1 g O_2 = 3.5 Cal (3.53 at R.Q. 1.0, and 3.28 at R.Q. 0.70).
(Note: At 0° C 760 mm pressure and 45° lat. 1 lit. CO_2 = 1.9652 g; 1 lit. O_2 = 1.4292 g; 1 lit. air = 1.2928 g; 1 lit. water vapor = 0.8038 g; 1 g water vapor = 1.2440 liters).

Calories
1 Cal = 1 kg-cal = 1000 gm-cal = 3.968 Btu at 60° F = 4185 joules
= 3086 ft-lbs = 426.7 kg-meters
1 cal = 1 gm-cal = 4.185 Joules = 42670 g-cm = 41.3 cc-atm = 0.04133 lit-atm
1 Btu = 0.252 Cal at 15° C = 778 ft-lbs

Work units (force × distance)
1 ft-lb = 0.1382 kg-met = 0.000324 Cal = 0.001286 Btu = 0.0005 ft-tons
1 kg-meter = 7.233 ft-lb = 0.002344 Cal = 0.009298 Btu
1 hp-hour = 1,980,000 ft-lbs = 641.3 Cal
1 joule = 0.2423 Cal = 10,000,000 ergs = 10,198 gm-cm = 0.00987 lit-cm

Power units, units work per unit time
1 hp (horsepower) = 33,000 ft-lbs per minute (or 550 ft-lb/sec or 1,980,000 ft-lbs per hour
= 4562.4 kg-m per minute
= 746 watts = 0.746 (about 3/4) kilowatt
= 2.1 liters oxygen/min = 10.7 Cal/min = 642 Cal/hr
watt = work at the rate of about 1/4 Cal/sec
kilowatt = 101.9 kilogram-meters per second
= 737.56 foot-pounds per second
= 1000 joules per second = 10,000,000,000 ergs per sec
$= \frac{1}{0.746} = 1.34$ hp
1 kg-m/sec = 9.81 watts
watt-hour = 0.85968 Cal
kw-hour = 859.68 Cal = 3412 Btu
1 lit-atm = 10.333 kg-m = 74.73 ft-lbs = 101.32 joules = 24.207 cal = 0.09607 Btu

Chapter 3

Energetic Efficiencies of Growth and Work Processes

> Waste not free energy; treasure it and make the best use of it. *Wilhelm Ostwald*

While there is no sharp dividing line between the two, it is convenient to divide agriculturally productive processes into two general classes (1) work and (2) growth, including "growth" of fat, milk, egg, wool, etc.

Thus defined, "growth" means the constructive or assimilatory synthesis of one substance at the expense of another (nutrient) which undergoes dissimilation. This is only one definition of growth; others will be considered in Chapter 16. In thermodynamic terms, the energetic efficiency of growth is the ratio of the growth *work* performed to the free energy expended. Traditionally, however, the energetic efficiency of growth is defined by the ratio of energy stored in the organism by the nutrient energy consumed.

3.1: Energetic efficiency of muscular work and the maintenance complication. Equation (2.2) indicates that the theoretically maximal efficiency of the Carnot heat engine is, under the usual temperature conditions, about 50 per cent. The maximal efficiency of actual heat engines is up to 20 per cent for steam engines, up to 25 per cent for gas engines, and 40 per cent for diesel engines. The average efficiencies are, of course, below maximal estimates.

Animals, however, operate not by virtue of changes or differences in temperature and pressure, as do heat engines, but by chemical energy operating at constant temperature and pressure, and the efficiency of isothermal converters, as of some electric transformers, approaches 100 per cent under certain conditions. Thus the efficiency of a slow-charging and discharging cadmium standard cell is almost 100 per cent [eq. (2.5)]. Furthermore, the free energy, ΔF, of the major body fuel, glucose, is practically identical with its heat of oxidation, ΔH, at constant temperature and pressure [eqs. (2.7a) and (2.7b)]. The efficiency of muscular work might, therefore, be expected to be much higher than that of a heat engine.

Actually, however, the *maximal* efficiency of muscular work in our horses, after deducting the "wastes" for maintenance and walking without load, was observed to be no higher than the *maximal* efficiency of the Carnot engine, not over 40 per cent (Ch. 24).

We measured *work performance* in horses by the method illustrated in Fig. 24.1 (p. 901), by multiplying the weight pulled, W, by the distance pulled, and the *energy expenditure* of these horses by the rate of oxygen consumption, assuming that virtually all energy was obtained by oxidation of glucose, as no doubt it was. The energy from the glucose thus oxidized [eq. (2.7)] is the heat of reaction, ΔH, which as previously noted is virtually identical with its free energy, ΔF.

No work was expended for moving the treadmill, which was actuated at desired speeds by an electric motor.

The energy expended by the animal included the following items:

1. Work accomplished
2. "Basal metabolism"
3. Heat increment of feeding (SDA)
4. Standing, above that of lying
5. Walking without load, above that of standing
6. Overcoming internal resistance (viscosity of muscle colloids)
7. Overcoming external resistance (wind, contact of feet with ground, etc.)
8. Useless incidental movements associated with pulling
9. Additional internal work of circulation, respiration, excretion, muscle tension, etc.
10. "Recovery" processes (see Ch. 6)

To simplify matters, we measured the oxygen consumption during: (A) standing, which covers items 2, 3, and 4; (B) walking without load, item 5; and (C) pulling the load, item 1. Item 10 was insignificant under the given conditions.

We then had three categories of efficiency:

$$\begin{array}{l}\text{Gross (or total[*])}\\ \text{efficiency of work}\end{array} = \frac{\text{useful work accomplished (Cal)}}{\text{O}_2\text{ consumed (Cal)}} \tag{3.1}$$

$$\begin{array}{l}\text{Net (or partial[†])}\\ \text{efficiency of work}\end{array} = \frac{\text{useful work accomplished (Cal)}}{\text{O}_2\text{ consumed during work above that of rest (Cal)}} \tag{3.2}$$

$$\begin{array}{l}\text{Absolute}\\ \text{efficiency of work}\end{array} = \frac{\text{useful work accomplished (Cal)}}{\begin{array}{l}\text{O}_2\text{ consumed during work above that of walking}\\ \qquad\qquad\text{at the same speed without load (Cal)}\end{array}} \tag{3.3}$$

The oxygen consumed in Calories, of course, corresponds to ΔH in thermodynamics.

It is obvious that the value of the gross efficiency [eq. (3.1)] will depend on the speed of work. The longer the time taken for performing a given quantity of work—that is, the longer the time of holding the muscles in a state of unproductive tension—the greater the overhead maintenance cost (items 2 to 4 above). On the other hand, the greater the speed of work, the greater the energy cost of the moving muscles in overcoming the internal resistance of the viscous colloids which make up the body. The gross efficiency of muscular work as a function of speed must, therefore, be of a rising and declining type (Fig. 24.3, p. 904) as it is for such machines as automobiles (Fig. 24.4, p. 905).

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[*] The term "gross" is preferred to "total" efficiency in order to avoid the implication that we are dealing with "total" energy changes.

[†] The term "net" is preferred to "partial" because of the well established usage for "net" (all reactions and efficiencies are in a sense partial).

The speed or time factor also affects the net [eq. (3.2)] and absolute [eq. (3.3)] efficiency because the energy expenditure for overcoming the internal resistance of the body colloids differs with speed. Speed of work affects the efficiency in animals in a manner somewhat analogous to that of temperature and pressure on the free-energy values of chemical reactions, or on the work efficiency of Carnot's engine.

It is important to note, on the basis of the data in Chapter 24, that for given physiologic work levels the efficiencies, gross, net, and absolute, are the same in (large) Percheron horses, (small) Shetland ponies and (still smaller) men. At a given *physiologic age and condition* the efficiency of work is independent of the size of the animal.

The observed maximal efficiency of muscular work in horses on treadmills will be shown in Chapter 24 to be of the order of 25 per cent for gross efficiency [eq. (3.1)], 28 per cent for net efficiency [eq. (3.2)], and 35 per cent for absolute efficiency [eq. (3.3)].

Fenn[1], and Hill and associates[2], reported efficiency computations of a different but related kind. Hill's computation on the theoretical maximum muscular work efficiency is based on the consideration of the energetics of an isolated frog-muscle strip. Hill imagines a reversible cycle—similar to the *PV* or Carnot cycle—in which the maintenance and related elements do not enter as complicating factors. Under such theoretical conditions, the "theoretical maximum work" was computed to be about 40 per cent approximately the same as for the Carnot engine.

Of this 40 per cent theoretical efficiency perhaps 60 per cent is, according to Hill, actually recoverable as work. What becomes of the remaining theoretically recoverable 40 per cent work energy? Hill thinks it is expended in overcoming the internal resistance of the body colloids. This resistance is wasteful of energy, but is useful to the animal because without it, he would "tear his tendons, break his bones, 'pull' his muscles, strain his joints".

Fenn computed a maximum gross work-efficiency of 23 per cent from data on the running of a man (carrying himself—no external load as in our horses). The work performed when running at maximum speed was computed to be at the rate of 2.95 hp and energy expended at the rate of 13 hp. Of the 13 hp expended 7.8 hp (60 per cent) was estimated to represent "waste of recovery", and 5.2 hp (40 per cent), "initial" (anaerobic) phase of muscle contraction. 2.95 hp of the "initial" energy (22.6 per cent of the total 13 hp or 57 per cent of the "initial" 5.2 hp) was used for work apportioned as follows: 1.68 hp (56.9 per cent of the 2.95, or 12.9 per cent of the 13 hp) for acceleration of limbs; 0.67 hp (22.7 per cent of 2.95, or 5.2 per cent of 13 hp) in friction of foot with ground; 0.10 hp (3.4 per cent of 2.95, or 0.77 per cent of 13 hp) for overcoming gravity; 0.13 hp (4.4 per cent of 2.95, or 1 per cent of 13 hp) in wind resistance. Unlike Hill, Fenn attributes much of the energy loss to overcoming external rather than internal viscosity resistance. Unlike Fenn's and Hill's running men, our working horses incurred no appreciable oxygen debt, so that Fenn's theoretic computations are not quite applicable to our working-horse data. None the less, these figures should be suggestive.

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[1] Fenn, W. O., *Am. J. Physiol.*, **90**, 343, 1929; **92**, 583, 1930; **93**, 433, 1930.

[2] Furusawa, K., Hill, A. V., and Parkinson, J. L., *Proc. Roy. Soc.*, **102B**, 28, 43, 380 (1927–8).

A basic difference between the work of an animal and of an engine is that the animal expends energy even when not working. The all-day or all-life energetic efficiency of an animal is, therefore, a complex function, among other factors, of the percentage of time spent for the work. The energy cost of maintenance tied up with the time factor is, aside from the economic aspects, a central problem in biology and agriculture which, necessarily, will frequently come up in this book, in various guises.

3.2: Energetic efficiency of growth and the maintenance complication. The growth-process category of biologic transformations is largely in the nature of storage: in higher animals and man the proteins, carbohydrates, fats, minerals, and vitamins in the diet are transformed into body, milk, egg, and so on, containing the same or derived substances. The situation is more complex in the case of bacterial and plant growth. The purely storage aspect of growth may be of no particular thermodynamic interest, but there is probably a *work* aspect to growth which is of thermodynamic interest.

Thus, the growth process involves creation and maintenance of: internal surfaces, differences in electromotive potentials, and differences in osmotic pressure, especially such as are involved in secretion, excretion, absorption, and in general transformation of amorphous nutrients to complex organisms. The configuration of the living organism, as for example, the newly-hatched chick, is on a quite different physico-chemical level from that of the yolk, white, and shell from which the chick developed, and it is, therefore, reasonable to assume that growth includes a work component involved in changing the configurations from that of food to that of organism.

In addition to the "work-of-growth" component, there are many irreversible free-energy losses which may be lumped together under the heading of "maintenance cost". Life is, so to speak, a flame, and simultaneously with the growth, building-up, process, there is a continuous oxidation, levelling, or catabolic process as predicted by the second law of thermodynamics. This "maintenance cost" is, perhaps, in part at least, the price paid for maintaining the thermodynamically unstable and statistically improbable complexly living, growing, evolving configuration, in the face of the opposite tendency of levelling disorganization to increase in entropy, as predicted by the second law of thermodynamics. Here speed of growth, size of body which has to be maintained, age on which speed and body size depend, and liberated catabolic enzymes enter as complicating elements in the estimation of the work of growth.

3.2.1: Efficiency of growth of bacteria: yeasts: and molds. The energetic efficiency of growth of bacteria, especially of autotropic bacteria, is surprisingly low. Burk[3] reported a gross efficiency of about 3 per cent for the bacterial conversion of atmospheric nitrogen to ammonia. Meyerhof[4] reported an efficiency of about 6 per cent for the assimilation of carbon from CO_2 (by *nitrobacter*) with the energy obtained from oxidation of nitrites to nitrates. Meyerhof's computations on the basis of the observed N/C ratio and assumption that the bacterial-body carbon has a combustion value of 113 Cal per gram atom of carbon (the same as in glucose, which according to Parks is 118 Cal per gram atom) was substantiated by Baas-Becking and Parks[5] on the basis of free-energy considerations. These authors also worked over Ruhland's[6] data with respect to the free-energy efficiency of bacteria which obtain their energy for reducing CO_2 into body tissue by oxidizing hydrogen. The efficiency of this assimilation is among the highest, about 26 per cent. (Eight mols H_2 are oxidized for the reduction of 1 mol CO_2; $H_2 + \frac{1}{2}O_2 = H_2O$, $\Delta F_{298} = -56$ Cal; the assimilation of 1 mol CO_2 to $C_6H_{12}O_6$ requires 118 Cal, $\frac{1}{6}$ of 709, see eq. (2.7c). Therefore, the efficiency is $\frac{118}{56 \times 8} \times 100 = 26$ per cent.)

As previously explained, the gross efficiency of growth of bacteria, as of other organisms, tends to increase with the speed of growth, since the major proportion of irreversible energy loss is associated with what is called "maintenance", a tax which must be paid regardless of whether or not the organisms grow. Thus, according to one observation[7], whereas during the first 10 days of growth of bacteria, when growth was most rapid, the gross efficiency was about 20 per cent, the growth efficiency during a 30-day period was 12.5 per cent because the organisms made very little growth in the last 20 days although the maintenance expense continued. Similar results were reported by Rubner[8] and others on other species of bacteria.

The gross energetic efficiency of yeast growth appears[9] to be of the order of 10 per cent, the exact value depending on the rate of growth.

Rubner[10], who was particularly interested in the influence of body size on maintenance cost, observed that the energy cost of maintenance, in terms of Calories per day per gram body nitrogen, is 1.0 for an adult man, 3.0 for a child, 3.0 for a dog, 15 for a mouse, 17 for a sparrow, and 20 to 60 for common bacteria, depending on species, temperature and so on. Other conditions being equal, the smaller the organism, that is, the greater the ratio of surface area to weight, the higher the maintenance cost per unit weight.

A possible objection to Rubner's reasoning as it relates to bacteria is that dead bacteria may have as great a "maintenance cost" as live ones, because

[3] Burk, D., *Intern. Cong. Soil Sci.*, **3**, 67 (1930).

[4] Meyerhof, O., *Pflüger's Arch. ges. Physiol.*, **164**, 353 (1916).

[5] Baas Becking and Parks, *Physiol. Rev.*, **7**, 83 (1927).

[6] Ruhland, W., *Jahrb. Wiss. Bot.*, **68**, 321 (1924).

[7] Tangl, F., "Energetik der Entwicklung," *Pfluger's Arch.*, **98**, 475 (1903).

[8] Rubner, M., "Energieverbrauch im Leben der Microorganismen," *Arch. Hyg.*, **48**, 206 (1904); **57**, 161 (1906).

[9] *Cf.*, for example, Brown, H. T., "Studies on Yeast," *Ann. Bot.*, **28**, 197 (1914).

[10] Rubner, M., "Kraft und Stoff in Houshalte der Natur," Liepzig, 1909.

as indicated by Buchner's[11] epochal discovery, cell-free bacterial extracts ferment sugar, and bacterial cultures always contain a large proportion of dead and autolyzing cells and considerable concentrations of the bacterial enzymes. Buchner's discovery, incidentally, marks the beginning of the modern era of enzyme chemistry. In brief, the fermentation speed is not necessarily a function of the bodily need, or indeed even related to the body, but varies with enzyme concentration, often liberated on the death of the organism.

It is possible that similar purposeless irreversible free-energy losses occur in bodies of higher organisms, a sort of tax to entropy, similar to that on conversion of heat to work in a heat engine. It is, at any rate, doubtful that the basal metabolism is simply the work of the physiological processes, such as that of circulation, respiration, secretion, excretion and muscle tonus. The energy expenditure for blood circulation under basal conditions is variously estimated from 5 to 15 per cent of the total; for excretion (kidney), 5 per cent of the total; for respiration, up to 15 per cent. Krogh[12] estimates that the energy for the functional activities made under basal conditions amount to about 25 per cent of the total metabolism. How is the remaining 75 per cent of the basal energy expended?

Brown[9] reported the interesting observation that the heat production of a population of non-growing yeast is about 100 times that of an adult man of equivalent mass; and that growing yeast generates considerably less heat per unit substrate fermented than do non-growing. This indicates the danger of extrapolating maintenance values from non-growing to growing organisms. Moreover, it may be illogical to do so because "maintenance" properly refers to a steady state, whereas growing organisms are not in a steady state.

The energetic efficiency of growth of molds is, apparently, much higher than that of bacteria and yeast. Terroine and Wurmser[13] reported a gross efficiency (including maintenance) of about 60 per cent, of the same order as of the chick and silk-worm embryos (see below) in contrast to an efficiency of 10 to 30 per cent for bacteria and yeast. The greater efficiency of molds may be attributed to more rapid growth and to greater control of catabolic enzyme activity. On the other hand, this difference may be due to methodologic research differences. While bacterial and yeast cultures contain a high concentration of catabolic enzymes liberated by autolyzing and perhaps living cells, the mold mycelia are harvested quantitatively before they autolyze. If a method were employed for harvesting bacteria and yeast cells prior to their loss or excretion of catabolic enzymes, the efficiency of the two might be the same.

[11] Buchner, H., "Alkoholische Garung ohne Hefezellen," *Ber. deut. chem. Ges.*, **30**, 117, 1110 (1897).

[12] Krogh, A., "The respiratory exchange of animals and man," p. 58, 1916.

[13] Terroine, E., and Wurmser, R., *Bull. Soc. Chim. Biol.*, **4**, 519 (1922).

The net efficiency (not including maintenance) of mold growth was estimated by Terroine and Wurmser to be about 72 per cent. But, as for yeast nd bacteria, one may question the significance of maintenance as obtained n a non-growing organism in relation to the maintenance cost of a normally growing one.

3.2.2: Energetic efficiency of prenatal growth. The bird, insect, or fish embryo is particularly suited for growth efficiency investigations because of he complete control of the organism, the definiteness of the nature of the nutrients, and the convenient relative isolation (Needham calls it cleidoic or closed-box system) from complicating environment. The gross energetic efficiency of growth of the chick up to hatching is obtained by estimating the combustion values of: (1) the egg, (2) the newly-hatched chick, and (3) the unused part of the egg, such as the left-over yolk and membranes.

Such measurements on the energetic efficiency of embryonic growth of the chick, silk worm, and fish were made by Tangl[14] and his pupils. Tangl's aim was to investigate what he termed *Entwicklungsarbeit*, the "work" of growth and development.

As in the case of bacterial growth, the gross efficiency, including maintenance, is easily determined, as indicated by the following example.

Combustion value of a hen's egg	87 Cal	100%
" " " hatched chick	38 Cal	43%
" " " unused material (yolk, membranes, etc.)	26 Cal	30%
Energy lost during incubation	23 Cal	27%

The gross efficiency is, then, $\frac{38}{38 + 23} \times 100 = 62$ per cent. The energy loss is $\frac{23}{38 + 23} \times 100 = 38$ per cent. How shall one explain the loss of the 23 Cal, or 27 per cent? According to Tangl, the 23 Cal represent the *Entwicklungsarbeit*, "work of development". This cannot be entirely true, because at least some of it must have been used for maintenance, and there is no simple method for differentiating the maintenance from the work components.

The following efficiency computation based on silk-worm data[15] yields very similar results.

Combustion value of a batch of unincubated silk-worm eggs	71.402 Cal	100%
" " " hatched larvae	31.879 Cal	44.65%
" " " unused material	22.291 Cal	31.22%
Energy lost during incubation	17.232 Cal	24.13%

Total efficiency, $\frac{31.879}{31.879 + 17.232} \times 100 = 65$ per cent;

energy loss, $\frac{17.232}{31.879 + 17.232} \times 100 = 35$ per cent.

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[14] *Cf. inter alia*, Tangl, F., *Pflüger's arch.*, **93**, 327 (1903). Tangl, F., and Farkas, K., *Id.*, **104**, 624 (1904). Tangl, *Id.*, **130**, 1, 55 (1909). For a comprehensive review, see Needham, J., "Chemical Embryology," vol. 2, Cambridge University Press, 1931.

[15] Farkas, K., *Pflüger's arch.*, **98**, 490 (1903).

Since the finished chick embryo is about 50,000 times the size of the silk-worm larvae, these two sets of data furnish an opportunity for comparing the influence of body size on the gross efficiency of embryonic growth of large and small embryos.

From the foregoing tables of Tangl and Farkas,

	Chick (%)	Silk-worm (%)
Energy loss during incubation	27	24
Gross efficiency, assuming that unused material did not participate in the growth process	62	65

Thus, the gross efficiency of embryonic growth is of the order of 60 to 65 per cent.

To equalize species differences with respect to weight, the efficiencies may be computed in terms of unit dry weight, as follows:

For the chick embryo, from Tangl,[18] we have

Combustion value of chick embryo	5.77 Cal/g dry weight
Energy lost during incubation	3.50 " " " "
Gross efficiency of chick growth	$\frac{5.77}{5.77 + 3.5} = 63$ per cent

For the silk-worm embryo from Farkas, we have

Combustion value of silk worm	5.33 Cal/g dry weight
Energy lost during incubation	3.10 " " " "
Gross efficiency of silk-worm growth	$\frac{5.33}{5.33 + 3.10} = 63$ per cent

The above comparison indicates that in spite of the size and species difference between chick and silk worm, there is no significant difference in gross efficiency of the two.

Similar efficiency values may be obtained from data on frogs[16]

Combustion value of frog embryo	5.5 Cal/g dry weight
Energy lost during incubation	5.3 " " " "
Gross efficiency of frog-embryo growth	$\frac{5.5}{5.5 + 5.3} \times 100 = 51$ per cent

and on the sea urchin.[17]

Combustion value of *Fundulus heteroclitus* embryo	4.8 Cal/g dry matter
Energy lost during incubation	3.3 " " " "
Gross efficiency of embryo growth	$\frac{4.8}{4.8 + 3.3} \times 100 = 59$ per cent

It is instructive to note that the fuel value per gram dry substance of chick embryo increases in sigmoid fashion from 5.1 Cal at the fifth day of incubation to 6.2 Cal at the end of the incubation period (21 days). The fuel value of dry unincubated egg-and-white mix is 6.94 Cal per gram.[18] This is a cogent argument against the use of increase in "dry matter" as index of growth in energy.

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[16] Fauré-Fremiet, E., and Dragoiu, J., *Arch d'Anat.*, **19**, 411 (1923).

[17] Glaser, O., *Biochem. Z.*, **44**, 180 (1912).

[18] Needham, "Chemical Embryology," vol. 2, p. 964.

It is significant that while gross energetic efficiency per gram dry matter is the same for the *finished* embryo in chick and silk-worm, there are changes in the efficiency during the period of growth, as indicated by the following table from Needham[18] based on Tangl's data on the chick.

Age (days)	3	5	7	9	11	13	15	17	19
Gross efficiency (%)	43	44	47	49	56	66	66	66	67

Needham explains this rise in efficiency (1) by possible decline of basal metabolism per unit weight with increasing weight, as inferred from Rubner's law; and (2) by extrapolation of Miss Stephenson's recapitulation theory to the effect that the enzymes are brought under continuously increasing control of the organism during ontogeny with consequently increased "disciplined" processes.

Instead of increased "discipline" growth, the apparently lower energetic efficiency in early embryonic life may reflect a greater speed of morphogenesis involving a greater work-energy component in comparison to the weight increment.

There is some confusion concerning the nature of this work energy of morphogenesis and growth. It may become resident in the formed structures, a species of configurational energy analogous to the energy stored on winding a spring. But existence of such configurational energy is somewhat hypothetical, since it is apparently not possible to measure it convincingly. Needham[18] has discussed the literature on this hypothetic organizational energy and appeared to conclude that it amounts to 4 per cent of the growth transaction. Bohr and Hasselbalch[19] reported that during the first few days of incubation of the chick embryo, heat was absorbed rather than dissipated, or at any rate, that there was a low heat production in comparison to oxygen consumption. This apparently "missing heat" may be due to endothermic reactions, to the retention of "organization energy" in the tissues[20]. Rapkine[21] observed unusually high respiratory quotients which he interpreted as indicating synthesis by coupled oxidation-reduction reactions as contrasted to simple combustion.

The situation is summarized in Section 1.3. For the present it may be noted that Tangl's research ignored the possibility that the energy expended for the "work" of growth and development may be structured in the tissue as potential energy (analogous, for example, to the energy expended for charging a battery or winding a spring); it assumed, on the contrary, that the energy expended for the "work" of growth and development is expended as heat analogous to that expended for rearranging the chairs in a room, in which case the potential energy of the chairs or room is not increased. Tangl, accordingly, measured the developmental energy by the difference in caloric values of the substrate (egg) and of the formed tissue (newly hatched chick, or silk worm, or fish). The heat thus measured by Tangl, however, included not only (1) the work of developing the organism, but also (2) the work of maintaining the organism. The net result of Tangl's work is that we are still ignorant of the magnitude of the organizational energy, since there is no method for separating (1) from (2) above.

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[19] Bohr and Hasselbalch, see ref. 6, Chapter 1.

[20] Terroine, E., and Wurmser, R., *Bull. Soc. Chim. Biol.*, **4**, 519 (1922); Meyerhof, O., *Biochem. Z.*, **35**, 280 (1911).

[21] Rapkine, L., *Arch. d'anat. microscopique*, **25**, 482 (1929).

The evidence seems to favor the viewpoint that much of the energy expended for organization is dissipated in the form of heat, as Tangl tacitly assumed, rather than structured into the organism. This may be inferred partly from the fact that unlike the structured energy in a battery or spring, the energy of differentiation is not reversible; differentiation processes are not reversible. Moreover, the energy in the formed tissue has not been shown to be higher than that of its constituent amino acids, carbohydrates and fats.

Several other sets of data substantiate the idea that much, if not all, of the organization energy is dissipated rather than structured. Thus, the pubertal-growth acceleration in children is associated with a metabolic acceleration[22]. The basal heat production in adult convalescent patients tends to parallel the speed of gain in weight during convalescence[23]. Rapidly growing rats (speed of growth controlled by litter size[24] and also by changing age[25]) have a much higher oxygen consumption or heat production—regardless of the reference base employed—than slowly growing rats. Rapid morphogenesis is associated with rapid metabolism.[26] The high basal heat production of adolescent children may, however, be attributed to a flare-up of high endocrine activity at that time. The high oxygen consumption of patients convalescing from emaciating diseases, or of rats on a high plane of nutrition, may be attributed to the latter factor (*SDA*, etc.) rather than to extra thermodynamic work of growth.

Tyler's[27] and Collier's[28] results are more convincing. Tyler reported that the oxygen consumption or energy liberation by the differentiating sea urchin varies with the amount of differentiation. Thus, the total oxygen consumption of two half-sized embryos up to the end of gastrulation is greater than of one normal-sized embryo. The two half-sized dwarf embryos are assumed by Tyler to expend the same amount of energy for maintenance and growth as one whole embryo. The difference in energy expenditure is assumed to result from the extra differentiation work involved in developing two embryos. Similar results were obtained by other methods of increasing developmental rates.

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[22] Du Bois, E. F., "Basal metabolism in health and disease," 1936. Topper, A., and Mulier, H., *Am. J. Dis. Child.*, **43**, 327 (1932). Lewis, C. A., *Id.*, **51**, 1014 (1936). Davenport, C. B., "Child Development," **10**, 181 (1939).

[23] Coleman, W., and Du Bois, E. F., *Arch. Int. Med.*, **15**, 887 (1915). Evans, F. A., and Strang, J. M., *J. Clin. Inv.*, **11**, 829 (1932).

[24] Brody, E. B., *Am. J. Physiol.*, **138**, 180 (1942).

[25] Kibler, H. H., and Brody, S., *J. Nut.*, **24**, 461 (1942).

[26] Barth, L. G., *Biol. Bull.*, **78**, 366 (1940); *Biol. Rev.*, **78**, 366 (1940).

[27] Tyler, A., *Pub. Staz. Zool. Napoli*, **13**, 155 (1933); *Biol. Bull.*, **68**, 451 (1935); *The Collecting Net*, **12** (July 10, 1937); *Biol. Bull.*, **74**, 99 (1938); **71**, 82 (1936).

[28] Collier, Jane G., "The relation between metabolism and morphogenesis during regeneration." Doctoral Dissertation, Dept. Zoology, University of Missouri, 1942.

Collier reported an 85 per cent increase in oxygen consumption at the peak of regeneration of the fasting worm *Tubifex tubifex*. Here the plane of nutrition did not enter as a complicating factor, as all animals were fasted. Measurements made of the oxygen consumption of intact and regenerating animals of the same size and in the same condition showed that there was an 85 per cent increase in oxygen consumption at the peak of regeneration. The obvious interpretation is that the extra oxygen consumption represents the "machine work" of regeneration.

3.2.3: Energetic efficiency of postnatal growth. It is not possible to measure the energetic efficiency of postnatal growth with the precision obtained on prenatal growth of the chick, because of the many variables influencing postnatal growth, such as differences in muscular activity, food supply and feeding habits, nature and quantity of food especially balance between nutrients, environmental temperature, and so on. There are, moreover, economic difficulties in making balance sheets of income and outgo of energy and especially determination of the composition of the gains.

Farmers estimate what they call efficiency—really a reciprocal function of efficiency—by the amount of feed consumed for making a given gain in weight. The terms "amount of feed" and "amount of gain" are poorly defined since the energetic equivalence of availability of feed and the energetic equivalent per unit body weight gain are highly variable. There is an enormous amount of such rough-and-ready data in the agricultural experiment stations. The following are a few illustrations of efficiency estimates for postnatal growth.

It is instructive to quote, by way of introduction, Rubner's[29] "law" of growth, to the effect that the amount of energy required for doubling the birth weight is the same per kilogram in all species, except man. About 4800 dietary Cal are required to construct a kilogram of normal body substance containing 30 g nitrogen and 1720 Cal. The energetic efficiency of the early postnatal growth is thus 1720/4800 × 100 = 35 per cent. The following is an example of Rubner's computations: Cal in the gain, 1500; Cal for maintenance, 2500; therefore, the energetic efficiency of growth is 1500/(2500 + 1500) = 37 per cent.

Rubner evidently refers in this example to what we call *net energy* of the feed. Indeed, he makes no mention of the feed used—only the energy in the gain and the (roughly estimated) energy cost of maintenance. The efficiency would, of course, be much lower if the energy in the gains were divided by the energy in the food consumed, and this value would vary with the feed category employed—gross, digestible, metabolizable, or net. To indicate the differences obtained by two comparable investigators, one may cite Lusk[30], who reported that pigs retain 20 per cent of their dietary calories during the first doubling of body weight, whereas Rubner stated that 40 per cent of the ingested energy is retained. Lusk reported the combustion value of the gain as 866 Cal per kilo, whereas Rubner stated that the combustion value of the gain as 1722 Cal per kilo. Yet, both Lusk and Rubner seem to agree that the milk energy required for a pig to double its birth weight is about twice the amount of energy deposited in the body.

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[29] Rubner, M., "Das Problem der Lebensdauer und seine Beziehungen zu Wachstum und Ernährung," 1908.

Attention should be directed to Kleiber's reasoning for assuming, as does Rubner and Lusk, that when other conditions are equal, productive efficiency is independent of body weight. According to Kleiber[31], the ratio of feed consumption to basal metabolism and maintenance is independent of body weight, and, therefore, the excess feed that may go for productive processes is independent of body weight. Thus the ratio of available calories ingested to basal metabolism is 4.4 in chicks, 4.2 and 5.6 in steers and 5.0 in a rabbit. In support of this, Kleiber[32] cited data[33] showing that 820-lb cattle and 114-lb sheep make the same gains per unit feed consumed during a 60-day period. The daily absolute gains were different, $2\frac{1}{2}$ lbs in cattle and $\frac{1}{3}$ lb in sheep, but both required 1040 lbs feed to gain 100 lbs weight. Moreover, it appears that rabbits and cattle are equally efficient converters of feed into live weight[34], presumably at equivalent physiologic ages.

Kleiber's observation that the ratio of maximum food consumption to basal metabolism, and also that the total productive efficiency, is independent of species and live weight cannot be generally true. An extreme deviation from this rule is the relatively very low ratio of food consumption to basal metabolism in children, as contrasted to that in growing farm animals. Another illustration is that pigs grow at a higher energetic efficiency than cattle because, presumably, pigs have a relatively greater feed-consumption capacity in proportion to maintenance cost than cattle. Lactating dairy cattle, of course, consume a great deal more feed in comparison to their maintenance cost than do beef cattle. Then, too, Kleiber's rule cannot hold for animals differing in physiologic age. Indeed, as noted in Chapter 1, whatever diferences there are in efficiency of different species and individuals at different ges must be due to differences in the ratio of feed consumption to maintenance ost.

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[30] Lusk, G., "The Science of Nutrition," Saunders, p. 569, 1928.

[31] Kleiber, M., *Tierernährung*, **5** (1933); also in Report on the Conference on Energy Metabolism, National Research Council, Committee on Animal Nutrition, Washington, 1935.

[32] Kleiber, M., "Problems involved in breeding for efficiency of food utilization," *Proc. Am. Soc. Animal Production*, Nov. 27, 1936.

[33] Rochford, L. H., "Some extension activities in California." *The Extension Animal Husbandman*, serial No. 42, 1936.

[34] Kleiber, M., "Kaninchen und Ochsen als Futterverwerter," *Die Tierwelt*, **36**, 437 (1926).

Generalizations of the type of Rubner's and Kleiber's necessarily involve arge margins of error. None the less they are useful, serving as pegs on which to anchor ideas, however insecurely.

The difference between Rubner's and Lusk's estimates of 35 per cent and 20 per cent efficiency, respectively, for early postnatal growth (during the irst doubling of body weight) of pigs, and Tangl's values of 62 per cent efficiency for prenatal growth of chicks does not imply a contradiction. It is entirely possible that the additional muscular, thermo-regulatory, digestive, excretory, and related activities characterizing postnatal life may involve a sufficient energy increment to account for this difference in gross efficiency.

Moreover, the increase in size of a given animal associated with increasing age would be expected to increase the energy cost of its maintenance and reduce correspondingly the total efficiency of growth unless this increase in maintenance is compensated by an increase in growth rate. In the case of different species, such as in cattle and chickens, there is such compensation and, therefore, nearly the same efficiency of growth, at *equivalent physiologic ages.* This is substantiated by the efficiency data cited on pp. 51–3.

But the increase in size associated with increasing age in the same animal is not thus compensated by increase in growth rate, with resulting decrease in efficiency of growth with increasing age or weight.

An interesting aspect of Rubner's generalization is that he excludes man therefrom. The human infant retains during the first doubling of body weight about 5 per cent of the dietary energy while the other species retain, according to Rubner, 35 per cent of the dietary energy. The reason for this exception will become clear on examination of the age curves of growth in man and other species in Chapter 16. In comparison to the body weight, the growth rate of the human infant is very much less than that of any other species; in other words, the maintenance cost of the human infant is greater in comparison to his rate of gain than is that of other species[35].

Let us next cite a few illustrations on the efficiency of growth of farm animals, and the most common laboratory animal, the rat. As previously noted, postnatal data are not well defined because of the differences in the availabilities of the various diets and differences in the energy equivalents of the weight gains (Ch. 2, 5). The following data[36] illustrate the variability in the energy content of the weight gains of "paired" rats, that is, rats apparently alike in every respect including nature and quantities of food consumed.

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[35] *Cf.* Lusk, G., "The Science of Nutrition," pp. 568–571. 1928.

[36] From Mitchell, H. H., and Carman, G. G., *Am. J. Physiol.*, **76**, 406 (1926).

Final weight (g)	Sex	Days on experiment	Gain in weight (g)	Combustion value of the gains (Cal/g)
118	M	56	25	0.32
134	F	56	38	2.66
165	M	56	68	2.44
169	M	56	73	2.56
228	F	156	162	2.35
241	M	156	180	2.84
185	F	156	119	3.26
223	M	156	157	3.10
280	M	156	215	2.37

Both the gains on a given food intake and the caloric values of the gains vary enormously in these homogeneous and pair-fed animals. The variability is likely to be far greater when comparing heterogeneous animals.

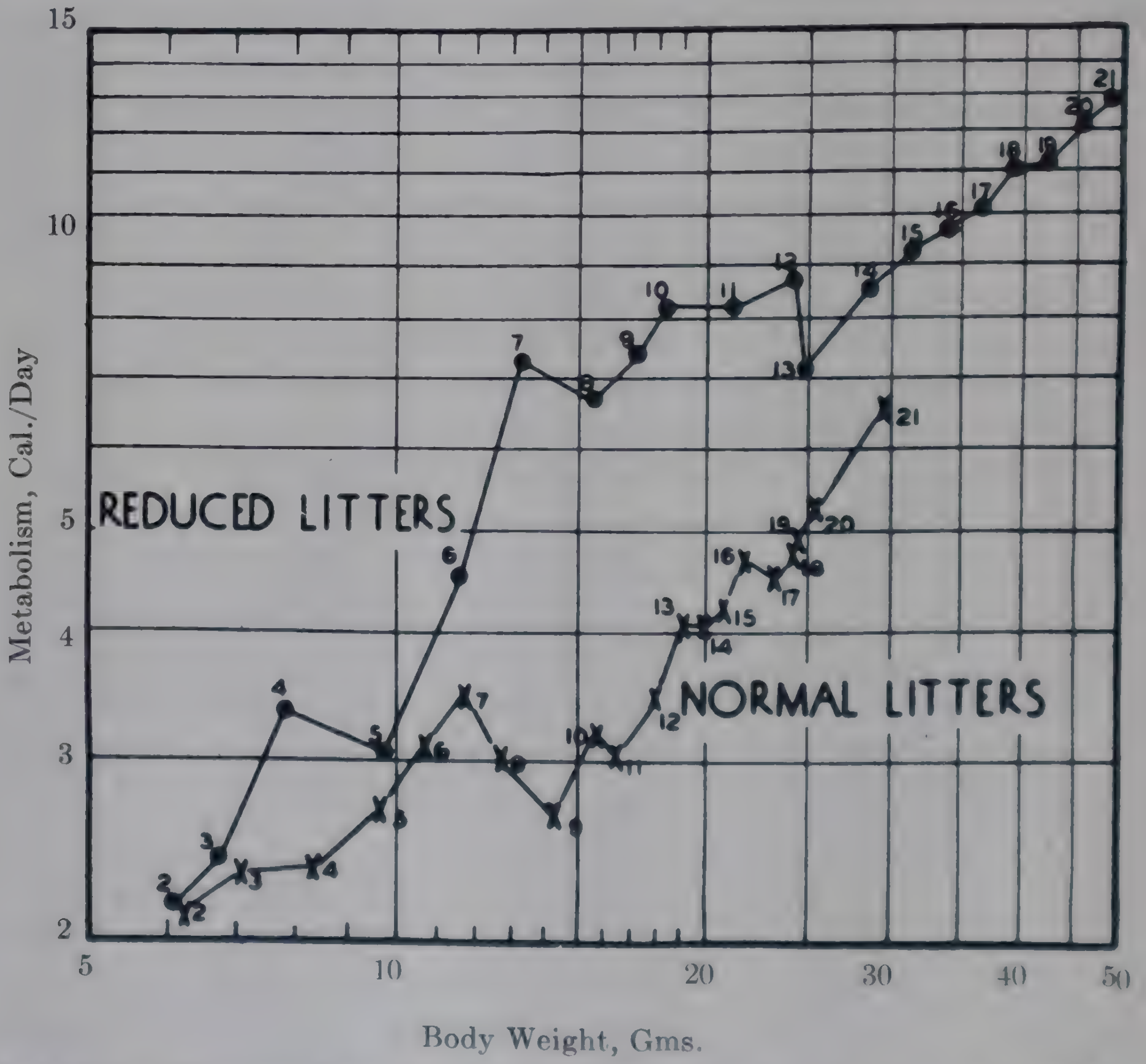

Fig. 3.1—The influence of the rate of growth (brought about by varying the litter size in suckling rats) on the heat production for *given weights*. The rapidly growing rats exhibited a higher heat production regardless of the reference base employed, than did the normals. Courtesy E. B. Brody and *Am. J. Physiology*, **138**, 180 (1942).

The following efficiency estimates, randomly listed from data by the same authors, illustrate the order of efficiency of growth of rats and its variability.

Initial weight (g)	Weight gain (g)	Metabolizable energy consumed (Cal)	Energy in the gains (Cal)	Gross efficiency of growth with respect to consumed metabolizable energy (%)
84	34	1302	8	0.6
89	76	1852	156	8.4
70	122	4642	352	7.6
70	194	5210	593	11.4
70	220	5539	751	13.6

Rubner's rule of 35 per cent efficiency does not apply to these rats, since these animals are beyond the age of first doubling of body weight.

The following estimates[37] on the gross efficiency of growth of Jersey cattle with respect to *TDN* consumed indicate an early efficiency near 35 per cent with a decline to 5 per cent at age 2 years.

Age (mos)	Live weight (lbs)	(1) Gains (lbs/day)	(2) Gains (Cal/day) (1) x 909	(3) *TDN* consumed (lbs/day)	(4) *TDN* (Cal) (3) x 1814	Gross efficiency (%) (2)/(4)
1	77	0.57	518	0.77	1397	37
2	100	0.77	700	1.53	2775	25
3	153	1.10	1000	1.83	3320	30
4	171	1.27	1154	2.43	4408	26
5	210	1.30	1182	3.26	5914	20
6	257	1.57	1427	3.96	7183	20
7	294	1.23	1118	4.61	8363	13
8	331	1.07	1118	4.76	8635	13
9	363	1.00	973	4.92	8925	11
10	393	1.00	909	5.45	9886	9
11	423	1.03	909	5.47	9923	9
12	454	0.93	936	5.98	10848	9
13	482	0.93	845	6.17	11192	8
14	514	1.07	973	6.59	11954	8
15	541	0.90	818	6.97	12644	6
16	570	0.97	882	7.32	13278	7
17	605	1.17	1064	8.04	14585	7
18	639	1.13	1027	8.17	14820	7
19	665	0.87	791	8.64	15673	5
20	700	1.17	1064	8.86	16072	7
21	726	0.87	791	9.03	16380	5

The following estimates on the gross efficiency of growth of Holstein cattle confirm those on the Jersey cattle.

Age (mos)	Live weight (lbs)	(1) Gains (lbs/day)	(2) Gains (Cal/day) (1) x 909	(3) *TDN* consumed (lbs/day)	(4) *TDN* (Cal) (3) x 1814	Gross efficiency (%) (2)/(4)	Lbs *TDN* consumed per lb weight gain (3)/(1)
1	108	0.87	791	1.24	2250	35	1.4
2	142	1.13	1027	2.17	3936	26	1.9
3	184	1.40	1273	2.15	3900	33	1.5
4	229	1.50	1364	3.22	5841	23	2.2
5	273	1.47	1336	4.13	7492	18	2.8
6	325	1.73	1573	5.08	9215	17	2.9
7	371	1.53	1391	5.74	10412	13	3.8
8	418	1.57	1427	5.91	10721	13	3.8
9	454	1.20	1091	5.93	10757	10	4.9

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[37] The weights are averages of cattle employed in our metabolism measurements. The *TDN* consumptions are averages of those given in Ragsdale, A. C., Univ. Missouri Agr. Exp. Sta. Bull. 338, 1934, and some other data.

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Age (mos)	Live Weight (lbs)	(1) Gains (lbs/day)	(2) Gains (Cal/day) (1) x 909	(3) *TDN* consumed (lbs/day)	(4) *TDN* (Cal) (3) x 1814	Gross efficiency (%) (2)/(4)	Lbs *TDN* consumed per lb weight gain (3)/(1)
10	488	1.13	1027	5.75	10793	10	5.1
11	531	1.43	1300	6.76	12263	10	4.7
12	572	1.37	1245	7.44	13496	9	5.4
13	610	1.27	1154	7.80	14149	8	6.1
14	654	1.47	1336	8.33	15111	9	5.7
15	698	1.47	1336	8.97	16272	8	6.1
16	740	1.40	1273	9.51	17251	7	6.8
17	781	1.37	1245	10.1	18321	7	7.4
18	826	1.50	1364	10.5	19047	7	7.0
19	863	1.23	1118	10.9	19773	6	8.9
20	899	1.20	1091	11.0	19954	6	9.2
21	942	1.43	1300	11.6	21042	6	8.1

The conversion factors employed, 1 lb *TDN* is equivalent to 1814 Cal (or 1 g *TDN* to 4 Cal), and 1 lb gain in live weight is equivalent to 909 Cal (or 1 g to 2 Cal), may be justly criticized, as the caloric equivalents per unit weight undoubtedly change with age and with other conditions. Thus, the combustion value per gram fat is equivalent to that of 2 g protein. In addition, 2 g protein is associated with about 6 g of water, while fat is not. An animal gaining protein alone would, therefore, gain 8 times as much weight, yet the same amount of energy as one gaining fat alone. This is an extreme illustration. It was reported[38] that rats fed a relatively high protein diet had an average combustion value of 1.8 Cal per g of tissue, whereas rats fed a low-protein diet had an average combustion value of 2.8 Cal per g (highest value was 3.6 Cal/g). The combustion value varies even for the dry tissue from 5.6 to 5.8 Cal per g. There are also variations in the energetic availability of *TDN* depending on many conditions. The tables, however, indicate the general trend.

The following estimates on steers indicate the nature of the energetic efficiency of beef production and how it is related to weight. As before, *TDN* is assumed to be equivalent to 1814 Cal per lb and 1 lb gain in weight to 909 Cal per lb.

Initial weight (lbs)	Weight gain (lbs)	*TDN* consumed (lbs)	Gross efficiency (%) (gain, Cal/*TDM*, Cal)
764	388	3400	5.7
412	488	2691	9.1
485	402	2195	9.3

The efficiency of beef production within the given limits is thus seen to be below 10 per cent. The apparent efficiency would be reduced still further by deducting the unedible part of the body weight.[39]

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[38] Johnson, S. R., Hogan, A. G., and Ashworth, U. S., Univ. Missouri Agr. Exp. Sta. Res. Bull. 246, 1936.

[39] Leitch, I., and Godden, W., (Imperial Bureau of Animal Nutrition, Tech. Communication 14, 1941) estimate that for fattening in beef animals, 9 to 10.7 cwt live-weight, the gross efficiency is 5.7 per cent with respect to dry matter; 16 per cent with respect to energy; 9 to 12 per cent with respect to protein.

The fact that efficiency is independent of body weight as such, but that it is rather related to physiologic age, is indicated by the following efficiency estimates on two groups of S.C. White Leghorn Chickens, one group growing very rapidly and the other growing slowly. The estimate of the fast-growing groups was based on unpublished data by Gustav Heuser; that of the slow-growing group on data by Card and Kirkpatrick (Storrs Station, Bull. 96). In spite of size differences the early-growth efficiency of chickens is very near that of cattle. Efficiency values of the same order were obtained for early growth of rats.

	Body weight (g)		% efficiency	
Age	Heuser	Card and Kirkpatrick	Heuser	Card and Kirkpatrick
1 day	39.9	37		
1 week	62.7	53	35	26
2	121.4	83	38	22
3	193	119	33	19
4	380	173	32	21
5	481	229	29	18
6	504	315	23	20
7	719	410	18	19
8	759	495	26	15
13		878		8.0
24		1490		2.5

It was assumed in the above computations for chickens that the metabolizable energy equivalent of the feed (not *TDN*) was 3 Cal/g, and 1 g weight gain is equivalent to 2 Cal. The results would, of course, differ with the conversion factors employed. (Heuser's ration was: yellow corn 57, wheat middlings 20, egg white 10, dried liver 7.5, cod liver oil 1, steamed bone meal 2, lime stone 1, salt 0.5.)

As previously noted, there is an enormous amount of data on growth and feed consumption, published and unpublished, in our agricultural experiment stations from which total efficiencies may be estimated, but which cannot be analyzed here.

3.3: Energetic efficiency of milk and egg production. The problem of energetic efficiency of milk and egg production will be discussed in detail in Chapters 21 to 23. This section compares, for the sake of completeness, the gross efficiency of milk and egg production with that of growth. The gross energetic efficiency of milk production in "good" dairy cattle and dairy goats is of the order of 33 per cent with respect to *TDN* consumed (assuming 1 lb *TDN* = 1814 Cal); and this efficiency, like that of growth at a given *physiologic age*, is roughly independent of body weight, or even of species as such. When other conditions are equal, it is approximately the same in dairy cattle, dairy goats, and white rats, as indicated in the table on p. 857. It is true that the milk production *per unit body weight* is greater in small than large animals, but the basal metabolism, or maintenance cost, *per unit body* weight is also greater in small than large animals with the net result that the two balance and the energetic efficiency is approximately independent of body weight. In this case Kleiber's rule holds. About $\frac{1}{3}$

of the consumed TDN (lb $TDN \times 1814$) is usually recovered in the milk of good dairy animals regardless of body size—if other conditions are equal.

The total energetic efficiency of milk production is comparable in magnitude to the total efficiency of very early postnatal growth, but it is very much greater than of beef production at later ages.

As egg is a more complex substance than milk, it requires more time for its elaboration, so that a greater proportion of the chicken's food would be expected to be used for maintenance in elaboration of egg than of an energetically equivalent quantity of milk with consequent lower total efficiency for egg than for milk production. The total energetic efficiency of egg production in good egg producers is approximately half that of milk production in good dairy animals.

It thus seems that, when other conditions are equal, the greater the structural complexity of the product the lower the energetic efficiency of its production. Milk, the least complex product, may be produced at the highest efficiency; this is followed by egg, and this by growth (meat).

3.4: Relation between the net energy category of feed and the efficiency of productive processes. The *net energy* of a feed is, by definition, the part transformed into the desired product: work, body tissue, milk, egg, and so on. The *net* efficiency of a productive process [eq. (1.2), excluding maintenance cost] should, therefore, be about 100 per cent with respect to the *net energy* category of feed ingested. The net efficiency of growth should be less if the efficiency is computed with respect to the *metabolizable*-energy category of feed (perhaps 70 per cent in cattle), and least (50 per cent in cattle) if it is with respect to the gross-energy category of ingested feed.

In discussing efficiency it is, therefore, imperative to specify what category of efficiency—gross or net—and what category of feed—gross, digestible, metabolizable, or net—is under consideration. The literature on productive processes is confusing, from the energetic-efficiency viewpoint, either because of poor specifications or because of lack of appropriate conversion factors under the given feeding conditions.

Thus, as explained in the preceding section, the *gross* efficiency [including maintenance cost, (eq. 1.1)] of milk production with respect to TDN consumption (assuming that 1 lb TDN is equivalent to 1814 Cal) is about 33 per cent. Yet Kellner's[40] balance experiments on three lactating cows yielded an efficiency of about 65 per cent.

Kellner, however, referred to the *net* efficiency [not including maintenance cost, eq. (1.2)], and the efficiency was with respect to the *metabolizable*-energy category of feed. It will be shown in Chapter 21 that the *net* efficiency of our data is of the same order as that of Kellner's.

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[40] See Armsby, H. P., "The Nutrition of Farm Animals," p. 493, 1917; Kellner, O., 5th Int. Kong. Milchwirtschaft, 1911; Kellner, O., "Die Ernährung der landwirtschaflichen Nutztiere," Berlin, 1919. Armsby and Moulton, "The animal as a converter of matter and energy," New York, Reinhold Publishing Corp., 1925.

Jordan[41] and Eckles[42], like Kellner, reported their milk-secretion studies in terms of *percentage utilization* of the *metabolizable* category of feed *above the maintenance cost*, which in our terminology is the *net* efficiency [eq. (1.2)] of milk production with respect to pounds TDN consumption (lb × 1814). Jordan's and Eckle's values were near those of Kellner's. Jordan reported 49, 57, and 64 per cent of "feed utilization"; Eckles reported 63, 68, 67, 51, 73, 60, 63 and 50 per cent utilization.

The *net* efficiency of milk production, not counting maintenance, is thus seen to be nearly double that of the *gross* efficiency, including maintenance. It is surprising that despite great differences in *gross* efficiency of growth, milk production, and egg production, the *net* efficiency, excluding maintenance [eq. (1.2)], appears to be roughly of the same order in all three processes, as will be shown presently for milk production (Ch. 21) and egg production (Ch. 23). Thus, Terroine and Wurmser[43], who worked over growth data by Kellner, Kohler, and Fingerling, concluded that the *net* efficiency of gains in weight ranged from 45 to 63 per cent in a cow and 52 to 84 per cent in a growing pig—values close to those for the *net* efficiency of milk and egg production.

The differences in the *gross* efficiencies of growth, milk production, and egg production may reflect differences in the time intervals required to produce unit energy in the form of milk, egg, and body gain, with corresponding differences in maintenance cost and consequently differences in gross efficiency. Time, and therefore maintenance, profoundly affect the gross efficiency of all productive processes.

Jordan[44] summarized the efficiencies of farm animals in terms of yield of edible solids per 100 pounds digestible organic matter consumed as follows:

Animal and product	Efficiency in terms of edible solids per 100 pounds of digestible organic matter in the ration
Cow, milk	18.0
Hog, carcass	15.6
Calf, carcass	8.1
Fowl, egg	5.1
Fowl, carcass	4.2
Steer, carcass	2.8
Sheep, carcass	2.6

This is probably a good practical representation of the *relative* total efficiencies of the several classes of animal converters as they existed in 1900. Biologically and energetically, however, the representation is vague. Thus, the caloric equivalence of "organic matter" obviously varies with its composition. Moreover, the amount of "edible solids" varies with the dietary habits of the consumer. Thus intestine (tripe) is a delicacy in some countries and offal in others, and biologically considered the energy equivalent of the offal is no less important than the edible parts.

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[41] Jordan, W. H., N. Y. (Geneva) Agr. Exp. Sta. Bull. 197, p. 24, and 20th Report, p. 29. See also his book, "Feeding Farm Animals," New York, 1901.

[42] Eckles, C. H., Univ. Missouri Agr. Exp. Sta. Res. Bull. 7.

[43] Terroine, E., and Wurmser, R., *Bull. Soc. Chim. Biol.*, **4**, 519 (1922).

[44] Jordan, W. H., "Feeding of Farm Animals", 1901.

This table underestimates the efficiency of modern dairy cattle, not only because the gross efficiency of milk production during the lactation period is nearer 33 per cent than 18 per cent, but also because beef animals yield only their bodies as edible end products for their rearing, whereas dairy animals not only eventually yield their bodies but also produce milk and calves. This, in effect, increases their life-time efficiency by spreading the cost of rearing over a much larger volume of edible product.

As previously noted, good dairy cattle, typified by experiment-station herds, produce milk at approximately 33 per cent gross efficiency with respect to *TDN* consumed—about $\frac{1}{3}$ of the *TDN* energy is recovered in the milk (assuming 1 lb *TDN* is equivalent to 1814 Cal). Egg is produced in comparatively good layers at approximately half this gross energetic efficiency, perhaps 16 per cent. The gross energetic efficiency of meat production declines rapidly with increasing age.

Pigs probably have a considerably higher gross energetic efficiency of growth[45] because they consume more concentrated feed in more available form—their "work of digestion" may be less—because they may have better appetites, consuming more nutritionally available feed above their maintenance level, or what is the same, they may have a relatively low maintenance level in comparison to their feed capacity. Pigs also have an exceptionally high dressing percentage in comparison to other animals as indicated by the following abbreviation from Whetham's extensive tables[46], the average of "Large White," "Middle White" and "Berkshire" breeds.

Live weight (lbs)	Carcass (%)	Approximate age (days)
60	69	97
70	71	105
80	73	114
90	75	122
100	76	130
110	77	138
120	77	147
130	78	155
140	79	163
150	79	171
160	80	180
170	80	188
180	80	196
190	81	204
200	81	213
210	81	221
220	81	229
230	82	237
240	82	246
250	82	254
260	82	262
270	82	270
280	82	279
290	82	287
300	83	295

While the dressing percentage is estimated to be about 75 per cent for average hogs, it is thought to be 56 per cent for calves (average live weight

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[45] To produce 1000 Cal live weight, fattening pigs need 77 per cent as much S.E. (starch equivalents) as bullocks. K. Breirem, cited by I. Leitch and W. Godden, Imp. Bureau of Nutrition, Tech. Communication 14, 1941.

[46] Whetham, Elizabeth O., "Pigs Breeders' Annual" (England), 1934–5.

190 lbs), 55 per cent for cattle (average live weight 940 lbs) and only 47 per cent for sheep and lambs (average live weight 85 lbs).

It is interesting to comment on the magnitude of the meat industry. The 1940 per capita meat consumption in the United States was about 150 pounds (67 lbs pork, 55 lbs beef, 7 lbs veal, 7 lbs lamb and mutton, 12 lbs lard). In spite of some 3 billion pounds more meat production in 1942, the war demands are expected to reduce the per capita civilian meat consumption to 135 pounds. The number of animals dressed in 1940 included about 78 million hogs, 15 million cattle, 10 million calves, and 22 million sheep and lambs. Dairy and poultry statistics will be cited, respectively in Chapters 21 and 23.

3.5: Summary. Agriculturally productive processes may be classified into work and growth processes, the latter including growth of tissue, fat, milk, egg, wool, and so on.

While the body is not a heat engine, the *theoretically maximal* efficiency of muscular work appears to be of the same order as of Carnot's heat engine, 40 to 50 per cent. The *actual gross maximal* [eq. (3.1)] efficiency of muscular work with respect to oxidized nutrients, which is roughly equivalent to the free energy, ΔF, of thermodynamics, is of the order of 25 per cent; that is, nearly $\frac{1}{4}$ of the nutrients oxidized in an animal working at top speed may be recovered in the form of useful mechanical work. The maximum *net* efficiency [eq. (3.2)], not including the standing maintenance cost, is about 28 per cent; the maximum *absolute* efficiency [eq. (3.3)], not including the energy expense when walking without a load, is about 35 per cent.

The growth process probably also involves work components, work of converting amorphous food materials, into organized tissue, but it is very difficult to estimate its magnitude partly because it is impossible to separate the energy expended for work from that for maintenance. The "maintenance" concept is also very complex, including many processes, some of which, as the catabolism of nutrients by enzymes excreted or liberated into the medium following the death of organisms, really have nothing to do with maintenance. Such unavoidable losses, of no benefit to the organism, may also occur in living organisms. Some of the maintenance energy represents real work—work of circulation, respiration, secretion, excretion, and so on; and some energy may be expended to "maintain" the thermodynamically unstable and "improbable" structural living configuration.

The gross efficiency of growth, including the maintenance complex, is 3 per cent for certain autotropic bacteria, about 10 per cent for yeast, 60 per cent for prenatal growth, 35 per cent for early postnatal growth, 5 to 10 per cent for beef production in later ages, near 16 per cent for egg production, and about 33 per cent for milk production. The net efficiency, which does not include the maintenance item is, of course, higher by the maintenance cost, and is roughly the same for all these processes.

The gross energetic efficiency of growth depends on the physiologic age interval under consideration because the older the animal the greater the maintenance tax in comparison to the productive increment. Thus Hammond[47] reported that whereas $22\frac{1}{4}$ lbs feed "weighed dry" is required to produce a pound of saleable beef for cattle finished at 3 years, it required only $11\frac{3}{4}$ lbs feed to make a pound of saleable beef for cattle finished at $1\frac{1}{2}$ years.

The efficiency of work, growth, milk production, egg production, and so on, is discussed historically and comparatively. Body size as such, when other conditions and especially *physiologic* age are equal, does not affect energetic efficiency, although it is an extremely important factor in the profit complex, which involves overhead expenses, such as the human labor of management, housing, and so on. The profit aspect—contrasted to the biologically energetic efficiency aspect—of body size, with special reference to milk production, is discussed in Chapter 22.

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[47] Hammond, J., "The Farmers' Weekly" (British), p. 13, Aug. 16, 1935.

Chapter 4

Specific Dynamic Action and Efficiency of Productive Processes

> The hypotheses which have been presented on specific dynamic action transcend one's power to coordinate them. *Graham Lusk*

4.1: Specific dynamic action, basal metabolism, and endogenous nitrogen excretion. As previously explained [eq. (2.10)], the *physiologic fuel value*, or the *metabolizable energy*, of a diet is composed of (1) net energy, or physiologically free energy, comparable to ΔF in thermodynamics, and (2) specific dynamic action[1] abbreviated to SDA, which is a tax to entropy, comparable to ΔS in thermodynamics, an extra heat increment incident to the nutritive process in total, including the energy cost of excretion of the end products.

One may say that the *resting* heat production of an animal in a thermoneutral environment is made up of two components: (1) *basal metabolism*, which is the irreducible energy cost of maintenance during complete rest, and (2) SDA, an energy waste incident to food utilization. *Basal metabolism* is, therefore, the resting energy metabolism in a thermoneutral environment in post-absorptive condition, uncomplicated by heat increments incident to food utilization or to low or high environmental temperatures.

Basal metabolism[2] is a convenient starting point for measuring the various heat increments, as heat increments of: fever, feeding, lactating, gestating, working, keeping warm in cold weather, and so on.

Endogenous nitrogen[3] *excretion* is similarly a convenient starting point for measuring various nitrogen-excretion increments as, for example, those due to food ingestion, and it is defined, empirically, as the lowest level of nitrogen excretion attained after an empirically defined time interval on a low-nitrogen but otherwise complete diet.

Both the basal energy and endogenous nitrogen levels are useful base values for computing the energy and nitrogen costs of maintenance. The relation of these basal values to total maintenance and to body size will be discussed in detail in Chapters 13, 14, and 15; they are here considered in their relation to the SDA problem.

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[1] Rubner, M., "Die Gesetze des Energieverbrauchs bei der Ernahrung," Leipzig, 1902; also *Z. Biol.*, **42**, 261 (1901).

[2] Du Bois, E. F., "Basal Metabolism in Health and Disease," 1936.

[3] Folin, O., "A theory of protein metabolism", *Am. J. Physiol.*, **13**, 117 (1905).

One method of measuring the *SDA* of protein or of amino acids is by the ratio of the heat increment above the basal level to the nitrogen excretion above the endogenous nitrogen level following a single meal, as illustrated in Fig. 4.3 and other methods are illustrated in Figs. 4.1 to 4.7.

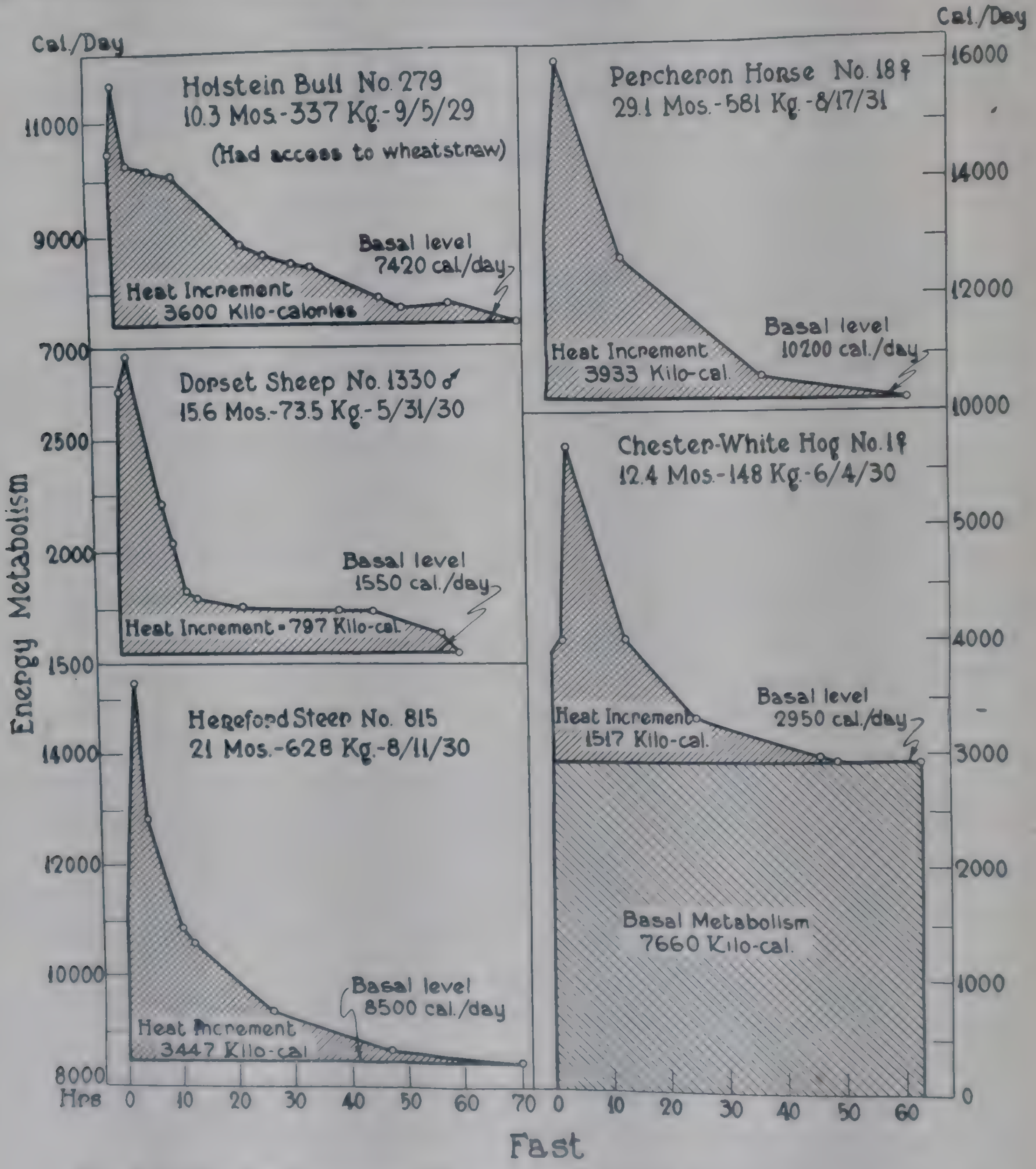

Fig. 4.1—The heat increment of feeding in several classes of farm animals

There is nothing particularly edifying about the term "specific dynamic action" outside of its historical connotation. Instead of the *SDA* designation, others are used, including calorigenic effect of food, heat increment of feeding, thermogenic effect, and thermal energy.

The calorigenic effect of drugs as of dinitrophenol[4], or of hormones such as thyroxine or adrenaline, consists in raising the metabolic activities of the body ells. Voit[5] suggested and Lusk[6] advocated Voit's theory that the nutrient agments likewise raise the metabolism of the body cells. This theory has, owever, apparently been disproved by the observation[7] that when the liver s removed, that is, when the deamination of protein is prevented (deamination of protein occurs mostly in the liver and to a less extent in the kidney[8]), utrients exert no specific dynamic effect; Lusk[9], therefore, bravely dis-arded his old teachings and adopted the thermodynamic viewpoint.

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[4] *Cf.* Brody, S., *Ann. Rev. Biochem.*, **3**, 341-3 (1934).

The fact that about 80 per cent of the resting *SDA* originates in the viscera[10] ubstantiates the theory that the *SDA* is due to the protein catabolism as uch rather than to stimulation of body cells.

The theory that *SDA* is the work of digestion[11] has been disproved by feed-ng bones and meat extract[12] and agar and cathartics[13] when no *SDA* was bserved. Moreover, injecting amino acids gives the same *SDA* as ingesting[14].

It is instructive to reflect on the fact that, although the phenomenon of heat ncrement of feed was observed over a century and a half ago[15], and although t has aroused enormous interest and elicited a great literature[6], there is no enerally accepted theory, nor indeed generally accepted quantitative definiion of *SDA*.

This is Rubner's[1] definition of *SDA*: If the *postabsorptive* energy expense of aintenance of a mature normal animal (dog) at *thermal neutrality* is 100 Cal a day, then if the animal consumes 100 Cal in the form of meat, its heat production will increase to 131 Cal for the day. The extra 31 Cal is the *SDA* of the 100 Cal of meat. If the animal is given 131 Cal, its heat production will ncrease to 137 Cal, and so on, as shown in the following table.

Relation between energy in the food and heat production by the animal.

	Protein Diet (Meat)		Fat Diet		Cane-sugar Diet	
Trial No.	Food energy	Heat production	Food energy	Heat production	Food energy	Heat production
1	0	100	0	112.7	0	100
2	100	130.9	112.7	114.3	100	106
3	130.9	137.3	114.3	114.5	106	106.4
4	137.3	139.3	114.5	114.55	106.4	106.42
5	149.3	139.9				
6	139.9	140.1				
7	140.1	140.2				

It appears from the above table that under the given conditions the *SDA* f lean meat is 40 per cent of the intake energy; of fat, about 15 per cent; of sucrose, about 6 per cent. That is, for example, of 115 Cal of physiologic fuel value (metabolizable energy) ingested in the form of fat, about 15 Cal is the entropy tax and 100 Cal is the physiologically free energy employed for maintenance or related useful purposes.

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[5] Voit, C., "Hermann's Handbuch der Physiologie," **6**, 209 (1881).

[6] Lusk, G., "The Science of Nutrition," 1928.

[7] Bollman, J. L., Mann, F. C., and Magath, T. B., *Am. J. Physiol.*, **78**, 258 (1926).

[8] Borsook, H., and Jeffreys, C. E. P., *J. Biol. Chem.*, **110**, 495 (1935).

[9] Lusk, G., *J. Nut.*, **3**, 519 (1931), and *Ergeb. Physiol.*, **33**, 103 (1931).

[10] Dock, W., *Am. J. Physiol.*, **97**, 117 (1931); **106**, 745 (1934).

[11] Zuntz, N., *Pflüger's Arch.*, **15**, 634 (1877); *Med. Klin.* p. 351 (1910).

[12] Lusk, G., *J. Biol. Chem.*, **13**, 155 (1912-13).

[13] Benedict, F. G., *Am. J. Physiol.*, **30**, 197 (1912).

[14] Weiss, R., and Rapport, D., *J. Biol. Chem.*, **60**, 513 (1924); Nord, F., and Deuel, H. J., *Id.* **80**, 115 (1928); Wilhelmj, Bollman and Mann, *Am. J. Physiol.*, **98**, 1 (1931).

[15] Lavoisier and Laplace, "Mémoire sur la chaleur," Mem. de math. et de Phys. de l'Acad. d. Sci., 1780, p. 355. Bidder, F., and Schmidt, C., "Verdauungsafte und Stoffwechsel," Leipzig, 1852.

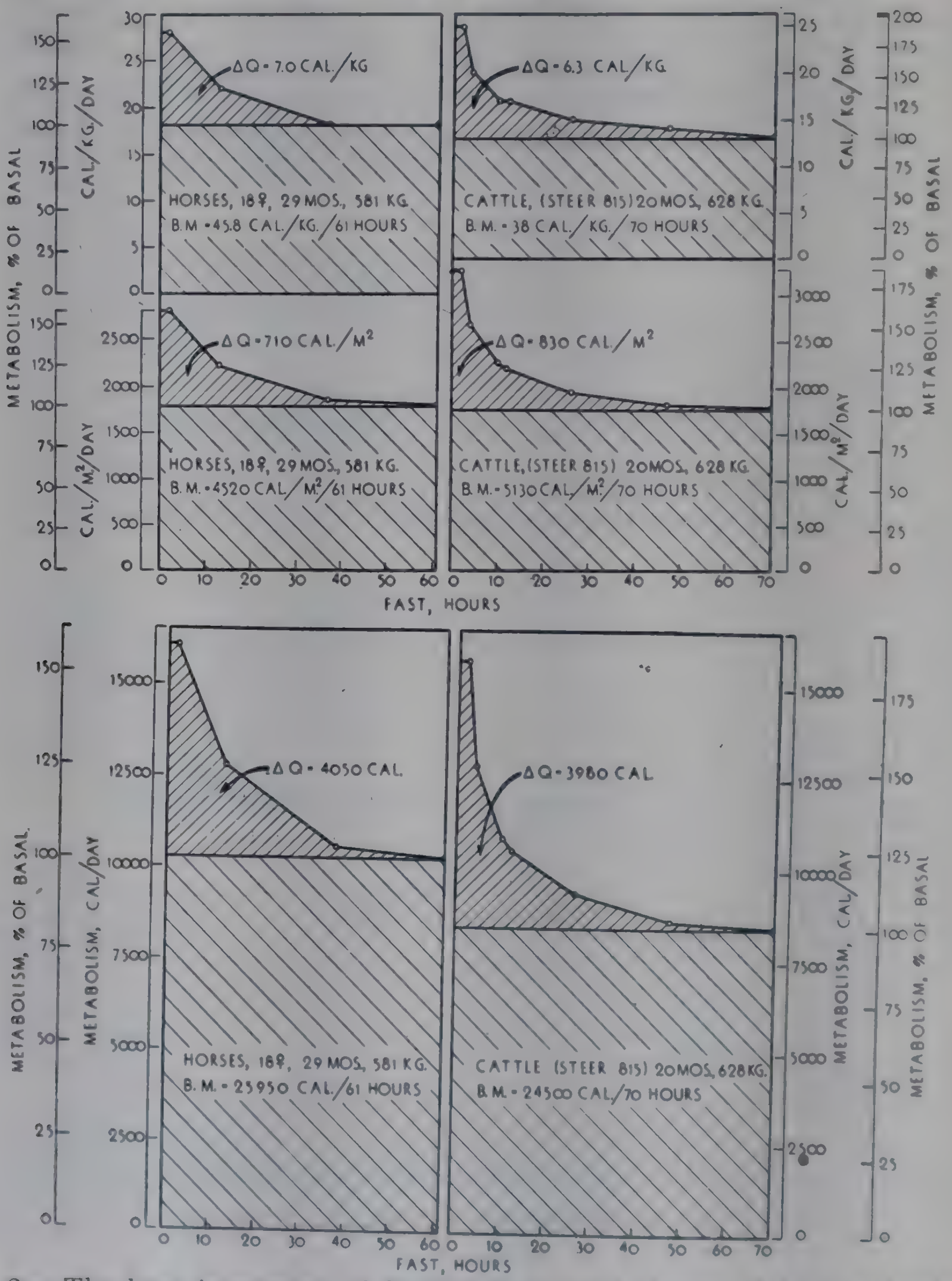

Fig. 4.2a—The heat increment of feeding in several classes of farm animals. The B.M. areas represent basal metabolism and the ΔQ areas the heat increment of feeding for the intervals shown on the time axis.

Murlin and Lusk[16] substantiated Rubner's values: "If what we now call the basal *metabolism* of a typical animal be 100 Cal, per day, and 100 Cal be administered to the animal of each of the several foodstuffs on different days, then the heat production of the animal after receiving meat protein will rise to about 130 Cal, after glucose to about 106 Cal, and after fat to about 104 Cal. These are typical average results." The typical animal is presumably a mature one.

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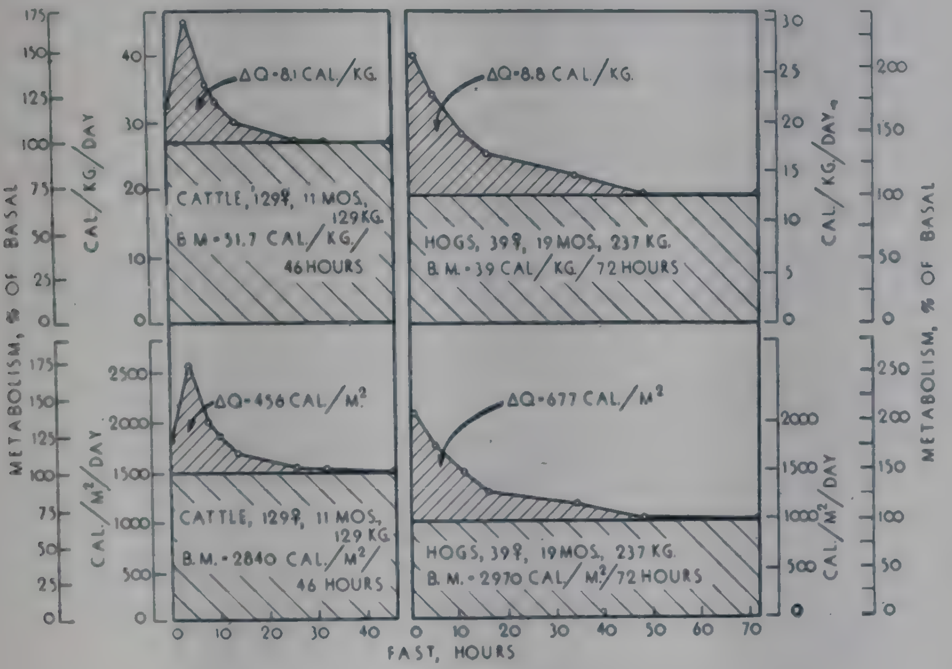
[16] Murlin, J. R., and Lusk, G., *J. Biol. Chem.*, **22**, 15 (1915). Murlin, *et al.*, *J. Nut.*, **12**, 613 (1936).



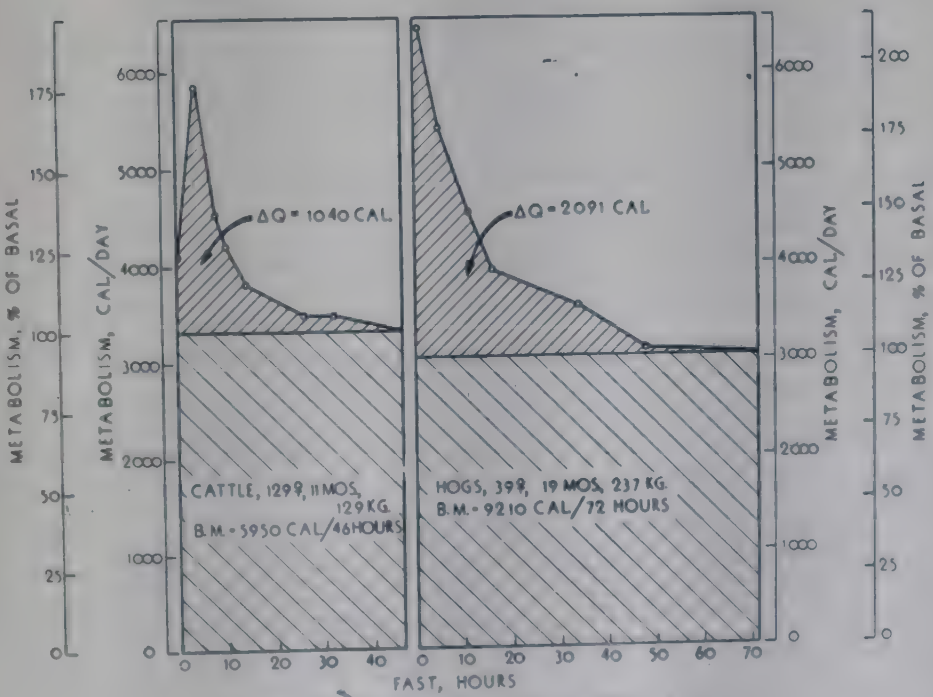


Fig. 4.2b—See legend of Fig. 4.2a.

Kriss, Forbes, and Miller[17] reported that the average heat increment (in 100-g rats) resulting from the *addition to a maintenance ration* (see Sect. 4.2) of casein, starch, and olive oil, respectively, expressed as percentages of the metabolizable energy of these supplements, were 31.4 per cent for casein, 22.5 per cent for starch, and 16.5 per cent for olive oil. These values, with reference to maintenance metabolism as base, were greater than with reference to fasting metabolism as base.

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[17] Kriss, M., Forbes, E. B., and Miller, R. C., *J. Nut.*, **8**, 509 (1934).

The literature on *SDA* is large and, as Lusk remarked in the quotation at the head of this chapter, very confusing. Rubner's theory[1] seems to be general enough, or perhaps vague enough, to embrace all thermodynamic theories. It is that the *SDA* represents the waste heat from the many intermediate and side reactions and oxidations incident to the nutritive processes. One may compare it to the waste in lumber manufacture—the trunks are utilized for the building industry but the branches and sawdust go into the brush fire; or one may compare it to the energy waste in a heat engine, part of which is free energy convertible to work and the rest is wasted, swelling the tide of entropy.

The contradictions in the literature on the *SDA* values of a given nutrient are due to the fact that the magnitude of the *SDA* of a nutrient is not a constant but, on the contrary, is highly variable depending on many circumstances, such as on whether or not the nutrient is stored or otherwise usefully employed; and this in turn depends on the balance between nutrients, plane of nutrition, environmental temperature, muscular or other productive activity, age, and so on.

Moreover, every amino acid has a characteristic *SDA*, a characteristic speed of utilization and catabolism, which influence the real or apparent end result. Thus, the *SDA* of the oxidative deamination of alanine is much greater than of the hydrolytic deamination of arginine. The liberation of nitrogen from the imidoazol ring of histidine is no oxidation. The *SDA* also depends on the deaminized residue.

The *SDA* value, moreover, depends on the reference base and units employed, whether it is represented in terms of heat produced to total nitrogen excreted, to nitrogen excreted above the endogenous, or above the maintenance level; to grams of nitrogen, or to equivalents of nitrogen, and so on.

By way of illustration, let us discuss the fate of the amino acid alanine when it is not stored in the body either because of excess ingestion or because of unbalance of the amino acid mix. In such case the amino acid is deaminized, producing urea, which is excreted by the kidney, and sugar, either stored in the body, converted to fat, or oxidized. The deamination may occur by three different methods: (1) oxidative; (2) simple; (3) hydrolytic.

$$(1)\quad \underset{\textit{(alanine)}}{CH_3\cdot CH(NH_2)\cdot COOH} + \tfrac{1}{2}O_2 = NH_3 + \underset{\textit{(pyruvic acid)}}{CH_3\cdot CO\cdot COOH} \rightarrow \text{urea} + \text{sugar}$$

$$(2)\quad CH_3\cdot CH(NH_2)\cdot COOH = NH_3 + \underset{\textit{(pyruvic aldehyde)}}{CH_3\cdot CO\cdot CHO} \rightarrow \text{urea} + \text{sugar}$$

$$(3)\quad CH_3\cdot CH(NH_2)\cdot COOH + H_2O = NH_3 + \underset{\textit{(lactic acid)}}{CH_3\cdot CHOH\cdot COOH} \rightarrow \text{urea} + \text{sugar}$$

In the first of the three reactions oxygen is consumed and, consequently heat is produced, equivalent to 4 Cal per g N catabolized. In the formation of urea from NH_3, there is also heat production, about 4 Cal per g N involved[18, 19], responsible for perhaps 20 per cent of the *SDA* of protein[20].

Then, too, the urea and other end products are excreted by the kidneys at a considerable energy cost, perhaps 1 to 2 Cal per g N excreted, accounting perhaps for 25 per cent of the *SDA* of the catabolized protein, attributed to kidney work[19, 21]. The efficiency of the kidney is estimated to be 2 to 5 per cent, 98 to 95 per cent of its energy expense being wasted as heat only, which heat is part of the *SDA* heat.

When the deaminized fragment is oxidized there may be, in the case of alanine, an additional heat production of about 30 Cal per g N excretion[19].

The heat liberated in deamination cannot be utilized for productive purposes; indeed, the heat of *SDA* is of the same nature as that given off as end product of muscular work. This is, of course, well known, having been observed by Rubner[22], Anderson and Lusk[23], Rapport[24], Meyer[25] and others. The *SDA* heat, like the heat of muscular work, can be useful only for keeping the animal warm in cold weather. Yet a working or otherwise productive animal on a given diet and level is likely to have a smaller *SDA* than a nonproductive one, because the nutrients are utilized at a higher rate for the productive process, leaving that much less for *SDA*. And in cold weather, the *SDA* spares the body from oxidizing body fuel to keep warm, giving the appearance of a decreased *SDA*. This is generalized by Rubner's *compensation theory*: there is a reciprocity between heat production by *chemical body-temperature regulation* and the *SDA*. Rubner found that the feeding of 320 g of meat to a dog at 7°C did not increase his heat production; but feeding 320 g meat at an environmental temperature at 30°C increased his metabolism (above the post-absorptive level) by 50 per cent. The reason that there was no apparent *SDA* at 7°C is that at this low temperature the "basal metabo-

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[18] Borsook, H., *Ergeb. Enzymfors.*, **4**, 32 (1935).

[19] Borsook, H., *Biol. Rev.*, **11**, 147 (1936). Borsook, H., and Winegarden, H. M., *Proc. Nat. Acad. Sci.*, **17**, 3, 13, 75 (1931).

[20] Borsook, H., and Keighley, G., *Proc. Nat. Acad. Sci.*, **19**, 626 (1933).

[21] The oxygen consumption of the kidney is said to be very high, about 9 per cent of that of the whole body at rest. However, Dock (loc cit) reported "that at least 80 per cent of the *SDA* is due to increased energy liberated by the hepatic cells during protein ingestion," and that "the oxygen consumption of the kidney was the same in rats on high and low protein intake, although the total oxygen intake of the former was 35 per cent greater than of the controls on the low protein diet." Borsook and Winegarden [*Proc. Nat. Acad. Sci.*, **17**, 3, 13, 75 (1931)], and Lublin [*Z. klin. Med.*, **109**, 371 (1928)] found an increased heat production as result of urea ingestion; but Carpenter [*J. Nut.*, **15**, 499 (1938)] found no effect on heat production in humans following ingestion of 30 or 40 g urea; nor according to Carpenter, did the following find increased heat production as result of urea ingestion: Tangl, *Biochem. Z.*, **34**, 1 (1911); Lusk, *J. Biol. Chem.*, **13**, 37 (1912); Grafe, *Deut. Arch. klin. Med.*, **118**, 1, (1915); Kocher and Torbet, *J. Biol. Chem.*, **95**, 427 (1932); Eaton, Cordill, and Gouax, *Am. J. Physiol.*, **113**, 37 (1935), also *J. Nut.*, **10**, 429 (1935); Rajzman, *Arch. internat. physiol.*, **43**, 423 (1936).

[22] Rubner, M., *S. B. Preuss. Akad. Wiss.*, **16**, 316 (1910).

[23] Anderson, R. J., and Lusk, G., *J. Biol. Chem.*, **32**, 421 (1917).

[24] Rapport, D., *Am. J. Physiol.*, **91**, 258 (1929).

[25] Meyer, F., *Arbeitsphysiol.*, **2**, 372 (1930).

lism" was higher on account of heat regulation, so that the heat of *SDA* replaced the heat of chemical regulation.

Another methodologic factor contributing to the *apparent* variation in *SDA* of protein is due to the failure to continue metabolism measurements, of both energy and nitrogen, until after the nitrogen and heat production return to the starting base level (Fig. 4.3). There are great differences in the rates of catabolism of different amino acids, different diets, in different individuals, under different conditions, and it is no easy matter to obtain *physiologically equivalent* values for the nitrogen and energy involved in the given *SDA* processes.

According to recent reviews[26], to which the reader is referred for details, some transformations of amino acids, as of glutamic acid[27], to urea (and other waste products) and to glucose are exothermic; others are endothermic, therefore, not realizable spontaneously, and requiring the driving force of a coupled exothermic reaction, and the *SDA* represents the difference between the energy produced and that used in the endothermic reaction. There is considerable disagreement among the experts[26] on all matters relating to *SDA*.

Carbohydrates undergo intermediate or preparatory stages, for example, phosphorylation (Ch. 6), on their path to storage (glycogen deposition) or oxidation, which changes involve a heat loss, the *SDA*. So do fats. Moreover, the conversion of fat to glucose[28] involves an energy loss of about 21 per cent, although the difference between the efficiency of fat and glucose utilization for work is only 11 per cent. Furthermore, physical changes, such as solution, osmotic pressure[29], and so on, involve additional heat liberation. The *SDA* of carbohydrates and fats may thus likewise be explained thermodynamically. Previous to his 1931 review, Lusk[9] attributed the *SDA* of carbohydrates exclusively to a plethora or mass-action effect. More recently the evidence, including that in Lusk's[30] laboratory, favors a thermodynamic interpretation. There is, in brief, no very good correlation[31] of *SDA* to blood-sugar level or even to the R. Q.[32]

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[26] Borsook[18]; Lusk[9]; Aubel, E., and Schaeffer, G., *Ann. Physiol. Physicochim. biol.*, **8**, 262 (1932); Krebs, H. A., *Ann. Rev. Biochem.*, **5**, 247 (1936); Wilhelmj, C. M., *Physiol. Rev.*, **15**, 102 (1935); Luck, J. M., *Ann. Rev. Biochem.*, **1**, 307 (1932); Lundsgaard, E., *Skand. Arch. Physiol.*, **62**, 223 (1931); Terroine, E. F., and Bonnet, R., *Ann. Physiol. Physicochim. biol.*, **2**, 488 (1926); **5**, 268 (1929); Brody, S., *Ann. Rev. Biochem.*, **3**, 295 (1934).

[27] Borsook, H., and Winegarden, H. M., *Proc. Nat. Acad. Sci.*, **17**, 75 (1931).

[28] Borsook, H., and Winegarden, H. M., "The free energy of glucose and tripalmitin," *Proc. Nat. Acad. Sci.*, **116**, 559 (1930).

[29] See, among others, Wilhelmj, Bollman and Mann, *Am. J. Physiol.*, **98**, 1 (1931); Lublin, A., *Z. Klin. Med.*, **109**, 371 (1928–29); Carpenter, T. M., and Fox, E. L., *J. Nut.*, **2**, 359 (1929–30); Carpenter, *J. Nut.*, **15**, 499 (1938); Lundsgaard, *loc. cit.*; Grollman, A., *Am. J. Physiol.*, **89**, 157 (1929).

[30] Dann, M., and Chambers, W. H., *J. Biol. Chem.*, **95**, 513 (1932).

[31] Mason, E. H., *J. Clin. Invest.*, **2**, 143 (1925–6); Rabinowitch, I. M., *Id.*, 143; Deuel, H. J., *J. Biol. Chem.*, **75**, 367 (1927); Baur, H., *Deut. Arch. Klin. Med.*, **164**, 202 (1929); Edwards, H. T., Margaria, R., and Dill, D. B., *Am. J. Physiol.*, **108**, 203 (1934); Carpenter, T. M., and Lee, R. C., *Am. J. Physiol.*, **102**, 659 (1932).

[32] Cathcart, E. P., and Markowitz, J., *J. Physiol.*, **63**, 309 (1927).

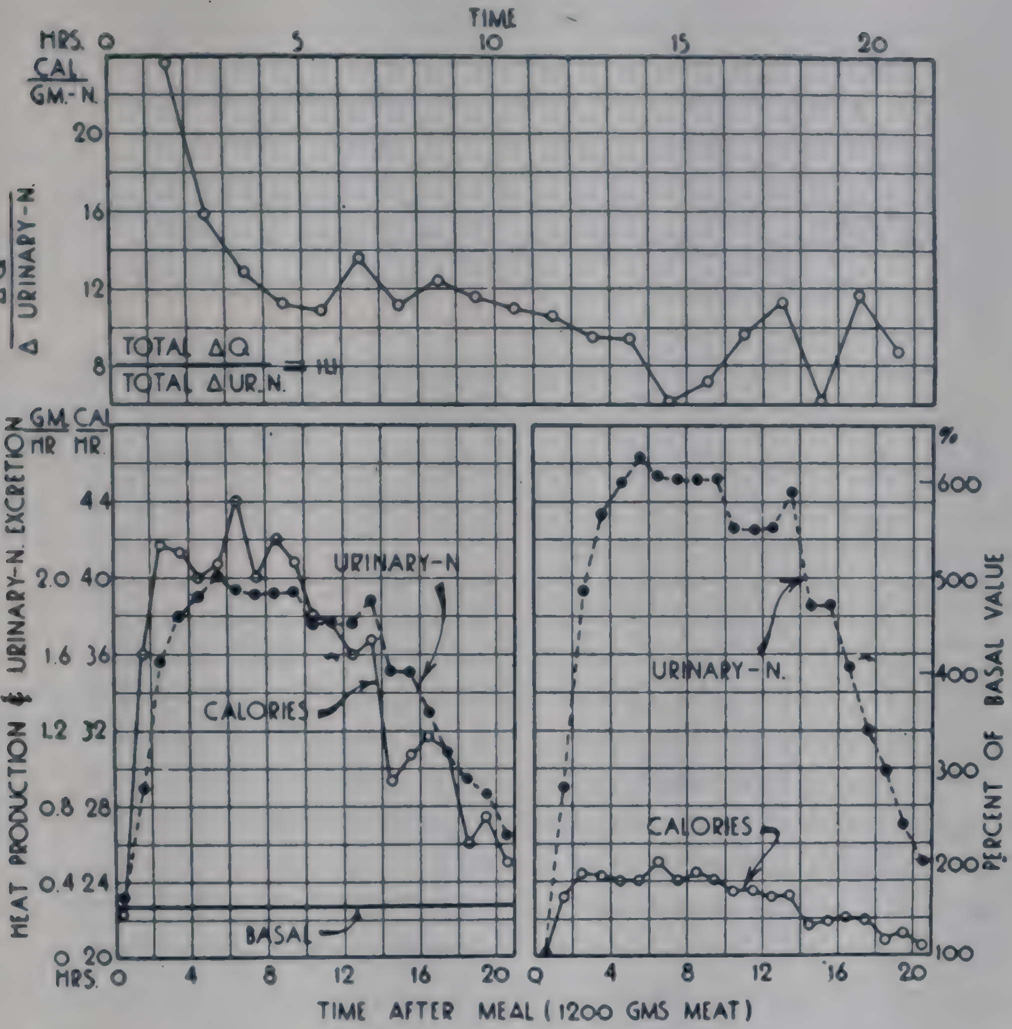

Fig. 4.3—The relation between heat production and urinary-nitrogen excretion plotted from data by Williams, Riche and Lusk (1912). The data were obtained on a female bull-terrier dog weighing 13.5 kg after feeding 1200 grams of meat and kept in a calorimeter at 26° to 27°C. The dog received no food for 24 hours preceding this feeding. The upper left chart represents the course of the ratio of Calories above basal (ΔQ) during given hours to nitrogen (in grams) above basal during the corresponding hours. The average ratio for the entire 21-hour period under observation is 11.1; that is, the total heat above basal produced during the 21 hours to the total urinary nitrogen excreted above basal during the same period was 11.1 Calories per gram of urinary nitrogen. (Williams, Riche, and Lusk say that "for the whole period the average increase in metabolism for every 100 calories of extra 100 calories of protein oxidized is 45 calories," and, "the ingestion of meat containing 900 calories in protein caused an increase in metabolism of 270 calories during a period of 20 hours, or the ingestion of 100 calories caused an increase of 30 calories in heat production.")

The lower left chart represents the heat production and urinary-nitrogen excretion in parallel manner; in the lower right chart the heat production and the urinary nitrogen excretion above basal are represented as percentages of the respective basal levels. This chart shows that the Calories reach a maximum value long before the nitrogen attains a maximum. It also shows that while the heat production was increased two times, the nitrogen excretion increased nearly six times. Note that the curve is not symmetrical about the maximum; the maximum occurs during the fifth hour, while the basal level is not reached again perhaps for 24 hours or longer.

4.2: Plane of nutrition and SDA. It is obvious that the *SDA* per unit food, especially of protein, will vary with the amount of nutrient taken and with the condition of the animal. Thus milk in moderate amounts ingested by a suckling animal[33] will have an inappreciable *SDA* because the nutrients, especially the proteins, are largely stored, and the stored nutrients as such have no *SDA*[1]. Likewise, a breakfast small enough so that the *SDA* of the dietary nutrients merely cancels that of the body nutrients which would be mobilized if the small meal were not taken, exerts no appreciable extra *SDA*[34]. Richardson and Mason[35] demonstrated that if only a maintenance ration is allowed, and that fed at two-hour intervals, the heat production will not rise appreciably above the basal level.

By the same logic, the *SDA* will depend on the reference base employed. Employing basal heat production and endogenous nitrogen as reference base (Rubner method) as most physiologists do (Fig. 4.1), the *SDA* will be less than if the maintenance heat production is taken as reference base, as some agriculturists do (Kellner method).

The Kellner method[36], as interpreted by Kriss[37], takes the maintenance metabolic level as reference base, and the *SDA* is evaluated not on the basis of one meal, as by Rubner's method (Fig. 3.1), but by feeding the animal for days first on the maintenance level, then for days on the maintenance-food plus the test-food. The difference in heat production between these two planes represents the *SDA* of the test-food. The results obtained by the two methods are different: the *SDA* of protein, fat, and carbohydrate is higher when using maintenance than when using fasting heat production as reference base[38]. The lower *SDA* obtained by the use of the fasting heat production as reference base is, as previously explained, attributed to the sparing of body nutrients from oxidation when food is fed to fasting animals. This is indicated by the fact that correcting for this sparing effect (on the assumption that the *SDA* of body nutrients catabolized in fast is the same as the dietary nutrients fed) raises the apparent *SDA* at submaintenance to near that obtained by the use of maintenance heat production as reference base.

Kriss' results with amino acids are, therefore, different from those obtained by the other investigators. Thus, Lusk and co-workers reported that while phenylalanine, alanine, and glycine have high *SDA*, glutamic acid, aspartic acid, and asparagine give negative results. Lundsgaard, Terroine and Bonnet, and others, reported that the *SDA* per gram nitrogen administered or excreted

[33] Rubner[1]; Hoobler, B. R., *Am. J. Dis. Child.*, **10,** 153 (1915). See also Necheles, H., *Am. J. Physiol.*, **101,** 79 (1932); Levine, S. Z., *et al.*, *Id.*, **33,** 722 (1927).

[34] Benedict, F. G., *Boston Med. Surg. J.*, **188,** 849 (1920); Soderstrom, G. F., Barr, D. P., and Du Bois, E. F., *Arch. Int. Med.*, **21,** 613 (1918). Wang, C. C., *Id.*, **46,** 316 (1930).

[35] Richardson, H. B., and Mason, E. H., *J. Biol. Chem.*, **57,** 587 (1923).

[36] Kellner, O., *Landwirtschaftlichen Versuchstationen*, **53,** 1 (1900).

[37] Kriss, M., "The specific dynamic effects of amino acids and their bearing on the causes of specific dynamic effects of proteins," *J. Nut.*, **21,** 257 (1941).

[38] Kriss, M., Forbes, E. B., and Miller, R. C., "The specific dynamic effects of protein, fat and carbohydrate as determined with the albino rat at different planes of nutrition," *J. Nut.*, **8,** 509 (1934).

is virtually the same for all amino acids. Kriss, on the contrary, using maintenance as reference base, reported that the important calorigenic factor is *metabolizable energy*—not nitrogen consumed or excreted (as reported by Lundsgaard, Terroine and others), and not the nature of the amino acids consumed (as reported by Lusk and associates). Kriss' results apparently contradict those of the preceding investigators. However, the contradiction may not be real, because Kriss' results are not comparable to those of the other investigators unless corrected for the difference in reference base employed.

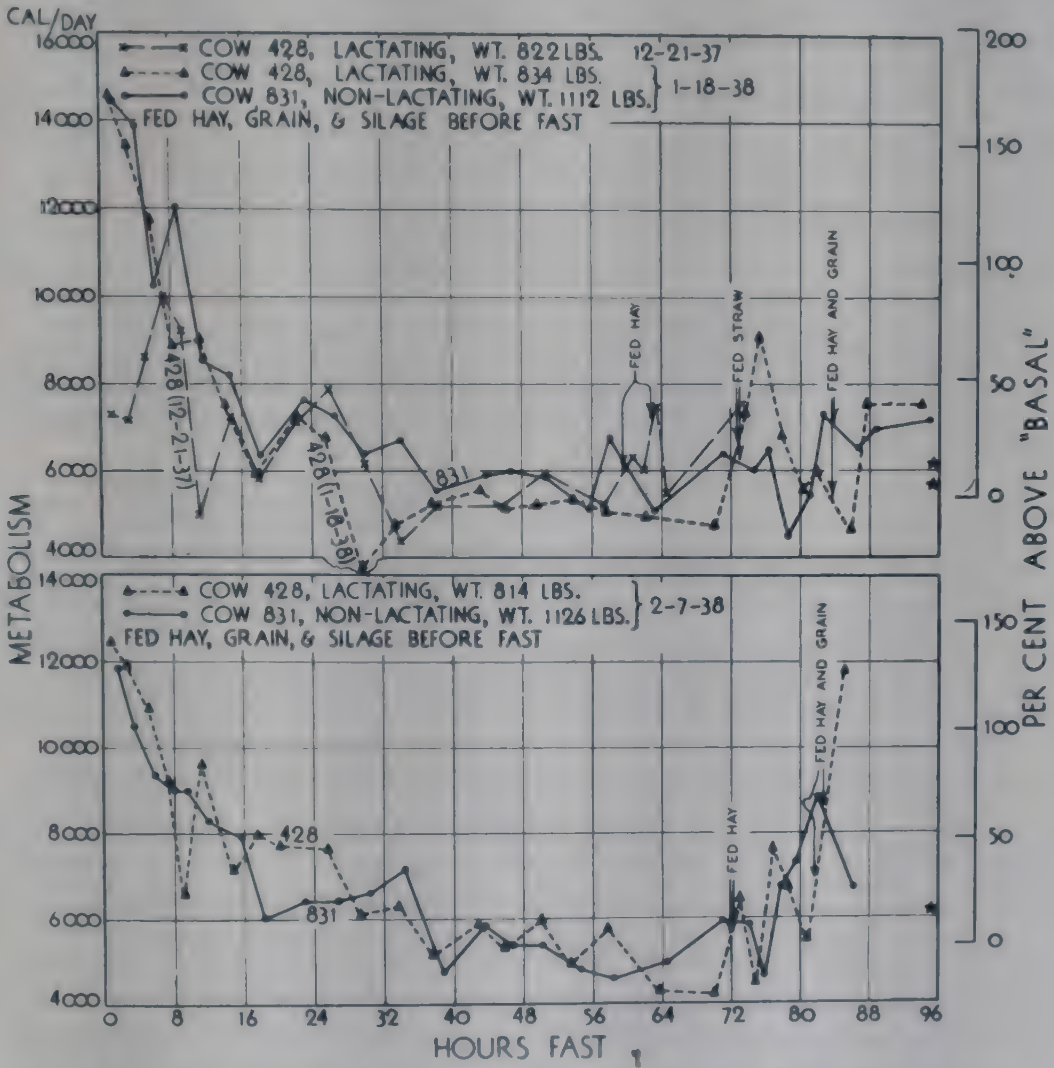

Fig. 4.4—The course of heat production in relation to feeding in cows.

The following table indicates that when maintenance is used as reference base, the carbon and hydrogen part of the amino acids is the major controlling factor in the level of *SDA*. This table harmonizes with the theory that at or above maintenance, the *SDA* represents the energy liberation of the intermediate chemical reaction of all nutrients, regardless of their nature.

SDA, in Calories, employing the maintenance level as reference base on rats. (Kriss[37])

Food Category	Glutamic acid 2.1 g	Alanine 1.8 g	Glycine 2.4 g	Glycine 1.8 g	Tyrosine 1.3 g	Aspartic Acid 2.0 g	Asparagine 2.0 g	Coefficient Variation (%)
Per 100 Cal energy metabolized	68	60	62	55	49	42	52	15
Per 100 Cal amino acid metabolized	92	82	69	65	49	63	67	20
Per 100 Cal gross energy	55	40	40	37	29	33	34	22
Per g amino-acid carbon metabolized	7	7	4	4	5	4	4	28
Per g amino acid fed	2.0	1.7	1.2	1.2	1.7	1.0	1.0	29
Per g amino acid metabolized	2.8	2.9	1.4	1.4	2.7	1.4	1.5	37
Per milimol amino acid metabolized	0.4	0.3	0.1	0.1	0.5	0.2	0.2	60
Per g extra urinary nitrogen excreted	29	13	7	7	19	13	7	60
Per g nitrogen fed	22	11	7	6	22	9	6	61

Forbes[39] suggested that the reference base for *SDA* computations should be neither basal (fasting) nor maintenance metabolism, but fasting heat production less the heat increment of utilization of body tissue catabolized during fast.

Forbes suggests the use of maintenance as the most practicable reference base, because "above maintenance, heat increments are measured with the minimum of ambiguity, with the heat production of energy equilibrium as the base value". Below maintenance the heat increments "are of mixed or indefinite significance by their contamination with energy expense of utilization of body nutrients catabolized".

To the present reviewer, however, it appears that the heat increment of a food above the maintenance level would also be "of mixed or indefinite significance by their contamination with energy expense of utilization", because the extra food above maintenance would be used for different purposes depending on the nature of the productive process. In the adult, the extra food would be used for fattening; in the young for growth; in the lactating animal for milk production, and so on, each involving a different energy expense of utilization and/or organization with resulting mixed significance.

There does not seem to be a definite *SDA* except under sharply defined reproducible conditions. The contradictory results and theories in the literature are due to the lack of definition of the influencing conditions. In the nature of the case, the *SDA*--and, therefore, the net energy—of a diet must differ with each of the influencing factors.

4.3: Nutrient unbalance and SDA. The absence of a limiting component from the metabolizable nutrients results in dietary unbalance and tends to increase the *SDA*.

Such an unbalance may be illustrated by the absence of one of the ten odd limiting amino acids from the dietary protein. As a result of the unbalance, the animal will be unable to synthesize its characteristic tissues or other products from the remaining amino acids. As the other amino acids are not utilized for protein synthesis, they are deaminized with consequently associated *SDA* as previously explained.

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[39] Forbes, E. B., Pennsylvania Agr. Exp. Sta. Bull. 415, 1941.

But other limiting nutritional factors may have a similar effect. Thus Mitchell[40] reported that lack of common salt reduces the utilization by chicken of the metabolizable energy of a corn ration. Several reports[41] indicate similar declines in utilization of metabolizable energy when phosphate is the limiting factor. While the influence of such deficiencies on *SDA* remains to be worked out, it is reasonable to assume that the *SDA* is increased because, by definition, the metabolizable energy is composed of net energy (the part

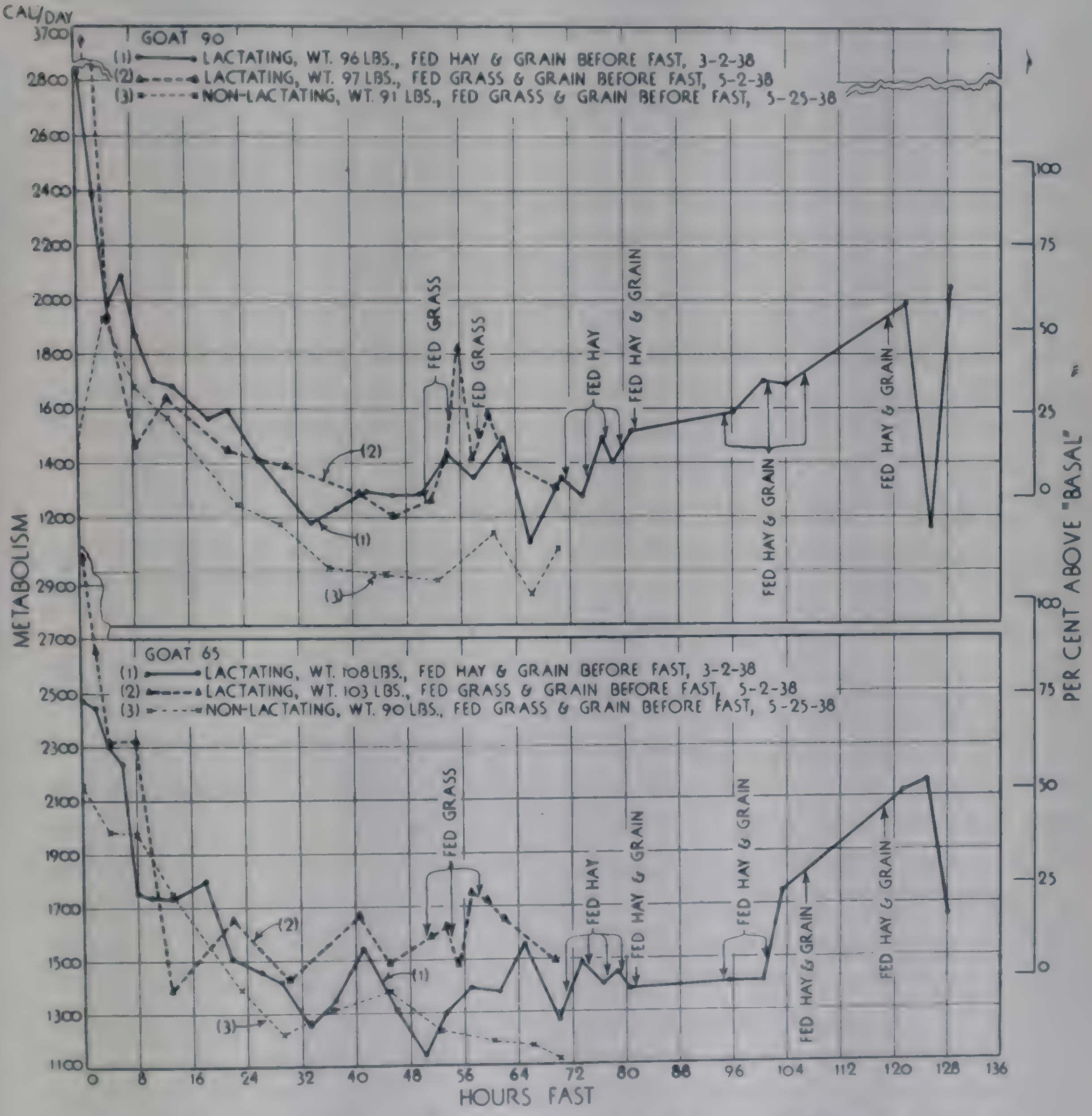

Figure 4.5—The course of heat production in relation to feeding in goats.

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[40] Mitchell, H. H., and Carman, G. G., *J. Biol. Chem.*, **68**, 165 (1926).

[41] Riddell, W. H., Hughes, J. S., and Fitch, J. B., Kans. Agr. Exp. Sta. Tech. Bull. 36, 1934. Kleiber, M., Goss, H., and Guilbert, H. R., *J. Nut.*, **12**, 121 (1936).

utilized for maintenance and production) and *SDA* (the part that is wasted), and decreased metabolizable-energy utilization necessarily means increased *SDA*.

4.4: Agricultural implications. The foregoing discussion indicates, first, that while the literature on *SDA* represents things that happen, the happenings are highly variable, depending on so many uncontrolled and uncontrollable factors that the results can be taken only as suggestive guides rather than as quantitative relations. Secondly, the results were obtained on dogs and rats, and it is evident that it is not possible to evaluate the *SDA* of individual amino acids or any simple nutrient in large farm animals, especially in cattle, with their basic diet of voluminous roughage and the associated fabulous flora and fauna that converts even urea to protein, and which ferments the rumen material with much heat production not differentiable from *SDA*.

Benedict and Ritzman published data on heat increment of feeding in steers[42] and sheep.[43] These increments appeared unexpectedly early and large. The theory given was that the anaerobic fermentation in the rumen results in early formation and absorption of short-chain fatty acids, such as butyric, which exert a heat-simulating effect of the Voit variety, prior to the protein effect.[43] The author has accumulated a great mass of similar data, some illustrations of which are shown in Figs. 4.1 to 4.7, on which he hopes to report in detail in the future.[44] More controlled data on steers will be discussed in the following chapter.

Whatever the theories, which are necessarily more or less works of imagination, the fact is that the heat increment of feeding in large farm animals, especially in ruminants, fed dietary unbalanced roughage, is huge. This heat increment could be reduced or perhaps abolished by feeding at appropriate intervals a perfectly balanced diet, as did Richardson and Mason.[35] But, of course, farm animals are not kept for maintenance but for production, and they are never fed proteins of 100 per cent biological value in particular or perfectly balanced rations with regard to needs in general. It would not be very profitable to feed milk to dairy cows or eggs to laying chickens. Moreover, the handling of bulky farm feeds, especially by ruminants, involves other energy expenses than those investigated by Rubner, Lusk, Terroine and others on dogs, rats, and frogs. The heat increment of feeding in farm animals is therefore large, about 20 per cent of the gross energy of the good customary "balanced" mixed rations consumed (much higher when fed poor roughage alone), or a heat production in dairy cattle under "normal" feed conditions of about 50 per cent above that in the fasting condition.

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[42] Benedict, F. G., and Ritzman, E. G., "The metabolism of fasting steers," Carnegie Inst. Washington, Pub. 377, 1927.

[43] Ritzman and Benedict, "Heat production in sheep," New Hampshire Agr. Exp. Sta. Tech. Bull. 45, 193; "Nutritional physiology of adult ruminants," Carnegie Inst. Washington, Pub. 494, 1938.

[44] See also data on goats: Magee, H. E., *J. Agr. Sci.*, **14**; on pigs, Capstick, J. W., and Wood, T. B., *Proc. Roy. Soc.*, **94B**, 35 (1922); Deighton, T., *Id.*, **95B**, 340 (1923); and *J. Agr. Sci.*, **19**, 140 (1929).

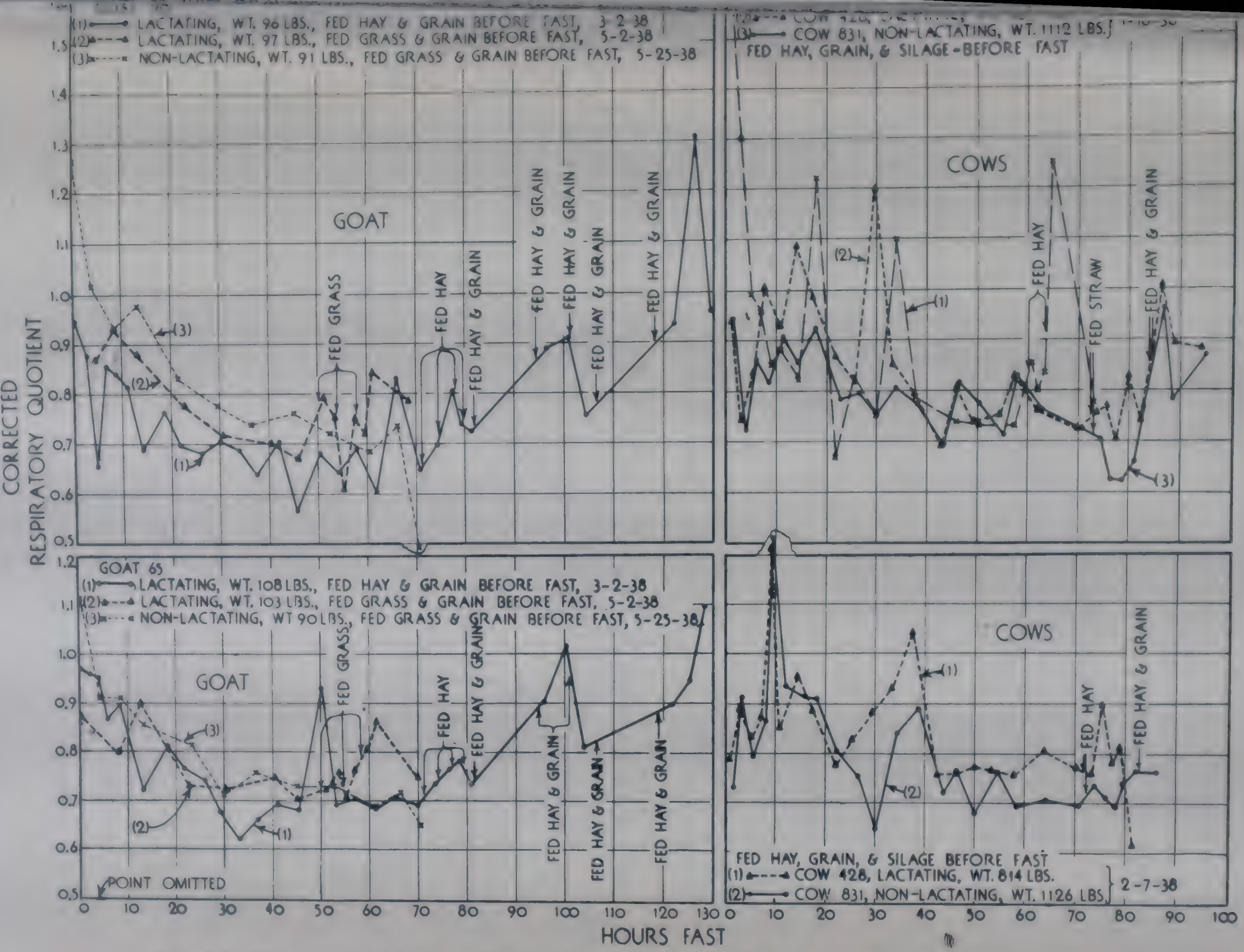

Fig. 4.6—The course of heat production in relation to feeding in a series of cows and goats.

The large heat increment is an effective protection against cold; this explains, in part, the ease of wintering livestock, especially ruminants, on a poor hay diet in the cold western states where the temperature is often −40° F. (Ch. 11). By the same token, the *SDA* is a serious burden in hot weather, popularly expressed by saying that heavy feeding, especially with protein-rich feeds, "burns out" the animal, and one of the major problems of animal husbandry is to keep down the summer body temperature in productive animals (Ch. 11) and, thus, maintain productivity.

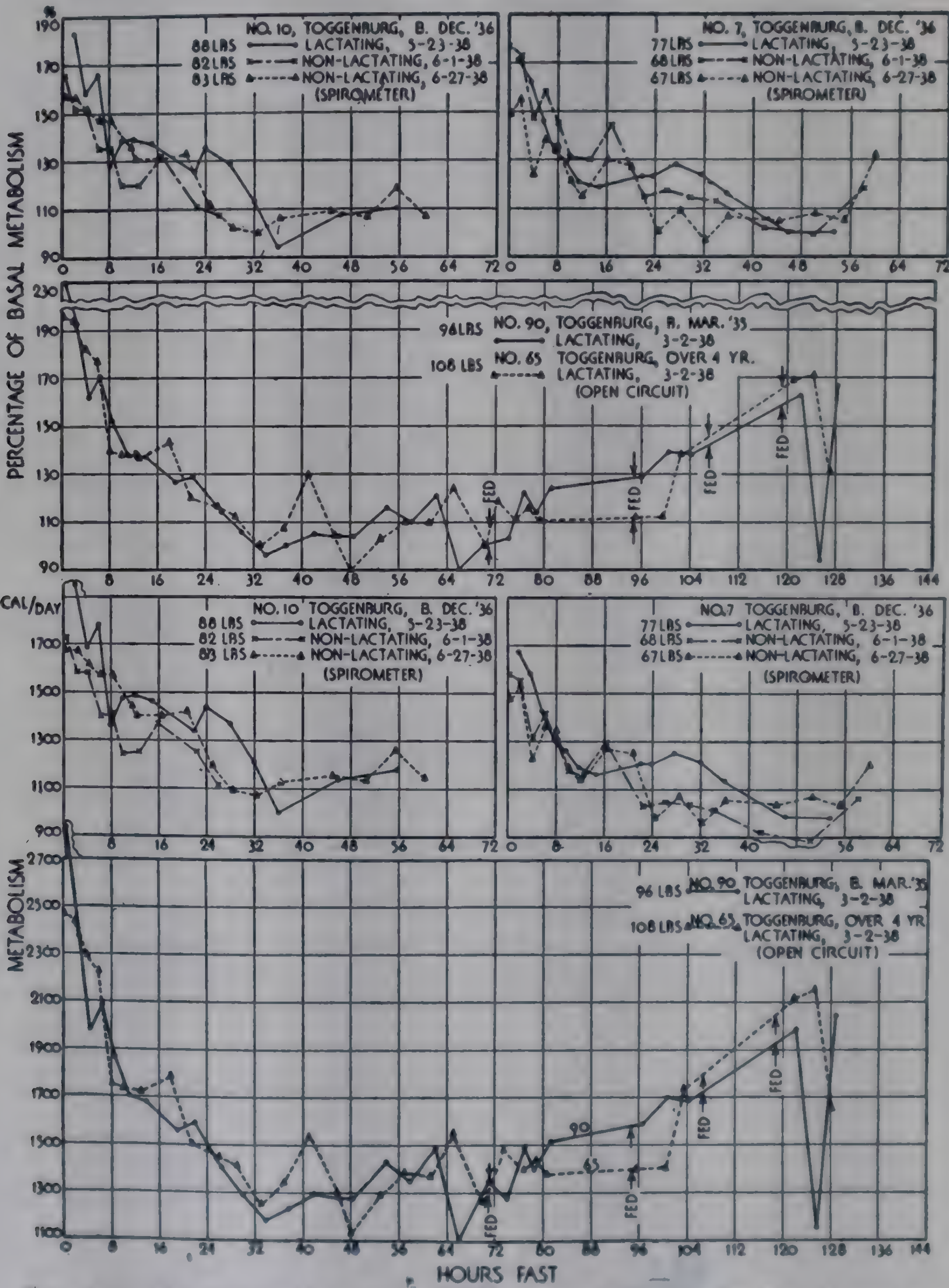

Fig. 4.7—The course of heat production in relation to feeding in goats.

4.5: Summary. The basal energy and nitrogen (endogenous) catabolism represent the irreducible caloric and nitrogen maintenance expenses respectively. Specific dynamic action, or *SDA*, or heat increment of feeding, or calorigenic effect of foods, represents the extra heat incident to the utilization of food or feed. The *SDA* of the extra protein is thus represented by the ratio of the resting heat production in a thermoneutral environment above the basal level to the nitrogen excretion above the endogenous level; or when using maintenance as reference base, it is represented by the ratio of the resting heat production above the maintenance level to the nitrogen excretion above the maintenance level. Similar representation may be made with respect to feed consumed or metabolizable energy consumed.

The *SDA* is very variable depending on the base level employed, on the plane of nutrition, on the balance between nutrients, on the nature of the productive process, and so on.

In cattle and sheep the *SDA* is further complicated by fermentation in the rumen, including heat generation in the rumen, a heat not differentiable from *SDA* heat. As a result, it is difficult to apply the great analytic literature on *SDA* from the thermodynamic viewpoint to the interpretation of the heat increment of feeding in farm animals, which must for the present rest on an empirical basis.

An analysis of the literature on dog and rat is, however, presented by way of background, giving special attention to the *SDA* following protein ingestion. If the ingested protein is not stored by the animal, its nitrogen is eliminated in the urine, and the carbon may be either stored in the body or oxidized. If all the carbon is oxidized, then, of course, since the physiological fuel value of protein is approximately 4 Cal/g, the heat increment of feeding of protein is about 4 Cal per g protein ingested, or $4 \times 6.25 = 25$ Cal per g of extra urinary nitrogen excreted. The usually observed *SDA* of protein (as of meat fed to a dog as shown in Fig. 4.1) is about 30 per cent of its metabolizable energy, from 8 to 12 Cal per g N excreted. The calorigenic effect of protein evidently varies with the nature and balance of the amino acids, and with the ability of the animal to store the protein or/and its deaminized fraction. Variations due to storage of protein may be eliminated by comparing calorigenic effects of a protein, not with the protein ingested, but with the extra nitrogen excreted. The extra heat will then represent the heat evolved in consequence of deamination, urea formation, and work of excretion of the nitrogenous waste products.

Attention is called to a few applications, such as the importance of the heat increment of feeding in outdoor wintering of animals in cold weather, or overheating in hot weather; the reduction of the *SDA* by frequent feedings of small meals, by muscular work, by balancing the nutrients in the ration, and so on.

The following chapter discusses the quantitative aspects of the influence of the plane of nutrition on the utilization of rations, with special reference to the heat increment of feeding in farm animals.

Chapter 5

Plane of Nutrition, the Principle of Diminishing Increments, and Efficiency

> The law of diminishing returns has been applied to phenomena which involve decrease in the per unit effect of some causal factor as the magnitude of the acting factor increases. *W. J. Spillman*

5.1: The principle of diminishing increments. If the dietary metabolizable energy is perfectly balanced with regard to all nutritional needs, and if it is fed below the maintenance level, it merely replaces what the liver would have delivered to the blood for maintenance, and the *SDA* (the extra heat increment incident to food utilization process in total) will be inappreciable; the *SDA* of the diet merely replaces that of the body nutrients, which would otherwise have been mobilized for maintenance needs. Above the maintenance level, however, the *SDA* progressively increases, or the net energy (the total food energy, less *SDA* and other food-utilization energy expenses) decreases for successive increments of food intake. The tendency for decline in utilization of successive dietary increments is an example of a ubiquitous phenomenon often generalized by the principle of diminishing returns, or diminishing increments, or the Weber-Fechner law, or the law of mass action (Wilhelmy, 1850).

This principle has been long recognized: "Increase in yield cannot be proportional to the fertilizer supplied, but it rises at a far smaller rate" (Justus von Liebig, 1860). "The man blessed with plenty of this world's goods requires a correspondingly larger increase in his good fortune than does the poor man in order to derive the same amount of pleasure". "The more additional means are expended, the less striking is the effect, which stretches out to almost vanishing fineness" (F. A. Lange, 1870), and so on.

Liebig[1] was probably the first to formulate this idea under the name of the "law of the minimum", which may be shown to be a special case of, if not identical with, the principle of diminishing returns. Liebig's formulation is based on the relation of fertilizer supply to plant growth, as was, much later, Mitscherlich's[2] and, independently, Spillman's.[3] It is evident that additions of successive units of fertilizer cannot increase the yield proportionally, unit yield for unit fertilizer; otherwise the yield could become infinitely great by infinitely large additions of fertilizer. Likewise, the consumption of successive food portions cannot benefit the consumer by equal amounts.

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[1] Liebig, J. V., "Die Grundsatze der Agriculturchemie", 1855; "Die Chemie in ihrer Anwendung auf Agrikultur", 1876.

A different biologic illustration of the principle of diminishing increments, discussed in detail in Chapter 16[4], is the decline in the time rate of growth in weight gains, dW/dt, with increasing age following the pubertal inflection. This may be represented by several equations, such as

$$\frac{dW}{dt} = ce^{-kt} \tag{5.1}$$

in which k represents the *relative* rate (or when multiplied by 100, the *percentage* rate) of decline of the differential time gains in weight, and e is the base of natural logarithms.

Here is an actual numerical illustration[5] of equation (5.1): The weight gains in successive months of a group of guinea pigs were observed to be 112, 90, 70, 56, 43, 35, 27, 21 $\cdots$ grams. The value of k is then approximately: $\frac{112 - 90}{112} = \frac{90 - 70}{90} = \frac{70 - 56}{70} = \frac{56 - 43}{56} = .22$, or 22 per cent per month; $k = .22$ (approximately). Having the value of k, the value of c is easily computed.[5a]

The *absolute* gains per unit time decline for successive months, but the *percentage* decline, $100k$, is constant. Since the gains in weight decline, the sign of k is negative.

Equation (5.1) may be written in several other forms, such as:

$$\frac{dW}{dt} = -k(A - W) \tag{5.2}$$

in which A is the mature weight, W, of the animal. The equation says in effect that the time rate of growth, dW/dt, is proportional to the remaining gains, $A - W$, yet to be made to reach the maximum weight, A. The farther from the mature weight, A, the more rapid the growth. As the animal gets older, the values of the gains remaining to be made, $A - W$, become progressively smaller, and so dW/dt becomes correspondingly smaller. The meaning of the numerical value of k is the same as in eq. (5.1).

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[2] Mitscherlich, E. A., "Das Gesetz des Minimums", *Landw. Jahrb.*, **38**, 537 (1909); "Zum Gesetz des Pflanzenwachstum", *Landw. Jahrb.*, **53**, 130, 167 (1919); *Fuhlings Landw. Z.*, **68**, 130 (1919); and many other papers.

[3] Spillman, W. J., "The law of diminishing returns", World Book Co., 1921; U.S.D. Agriculture Tech. Bull. 348, 1933.

[4] See also, Brody, S., "Growth Rates", Univ. Mo. Agr. Exp. Sta. Res. Bull. 97, 1927.

[5] Brody, S., "Genetic growth constants", *J. Gen. Physiol.*, **8**, 237 (1926).

[5a] Becker, G. B., Smithsonian Mathematical tables, #1871, Smithsonian Institution, Washington, 1924 (pp. 226 and 263).

The *differential* (time rate) equations (5.1) and (5.2) may be written in the *integral* (cumulative) form, giving not the differential weight gains, dW/dt, but the total body weights, W, as a function of age, t,

$$W = A - Be^{-kt} \tag{5.3a}$$

In some cases, or from some viewpoints, A equals B (that is, $W = 0$ when $t = 0$), in which case the equation is

$$W = A(1 - e^{-kt}) \tag{5.4a}$$

Equations (5.1) to (5.4) are growth equations; but such growth (following puberty) is evidently an illustration of the principle of diminishing increments: the weight, W, gets larger with increasing age, t, but the increases per unit time become progressively smaller. Time, t, may be formally considered as the "causative agent", which has less and less effect on increasing the body weight. The physiologic significance of a physical time[6] unit declines with increasing age (Ch. 19).

Instead of body weight, W, and age, t, we may relate milk-energy production, FCM (which represents milk corrected to 4 per cent fat, having a combustion value of 340 Cal per pound, or 750 Cal per kg), to TDN (digestible nutrient) consumption. In this case equation (5.3) becomes

$$FCM = A - Be^{-k(TDN)} \tag{5.3b}$$

The FCM yield rises with increasing TDN production, but at decreasing increments; the successive TDN units consumed elicit progressively smaller milk (FCM) production increments.

Instead of discussing particular products, as milk, or egg, or fat, or work, we may say that as the dietary gross energy, Q_g, consumption is increased by equal units, the net energy, Q_n, that is, the magnitude of the energy recovered in the given product, become progressively smaller; that is

$$Q_n = A - Be^{-K(Q_G)} \tag{5.3c}$$

In addition to its application to the effect of fertilizer increments on crop-growth increments, previously cited, this principle has been used in agriculture for relating the effect of feed-intake on its net energy value[7], on growth rate[3, 8], and on milk production.[9]

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[6] Brody, S., "Relativity of physiologic time", *Growth*, **1,** 60 (1937).

[7] Brody, S., and Procter, R. C., "Influence of the plane of nutrition on the utilizability of feeding stuffs", Univ. Missouri Agric. Exp. Sta. Res. Bull. 193, 1933.

[8] Jull, M. A., and Titus, H. W., "Growth of chickens in relation to feed consumption", *J. Agr. Res.*, **36,** 541 (1928); **48,** 817 (1934); *Poultry Science*, **11,** 74 (1932). Titus, *Poultry Sci.*, **7,** 254 (1928). Hendricks, W. A., "Fitting the curve of the diminishing increments to the feed consumption-live weight growth curves", *Science*, **74,** 290 (1931). Hendricks, Jull, and Titus, *Id.*, **73,** 427 (1931).

[9] Jensen, E., Klein, J. W., Rauchenstein, E., Woodward, T. E., and Smith, R. H., "Input-output relationships in milk production", U.S.D. Agriculture, Tech. Bull. 815, 1942.

Spillman[3] and Jensen[9] employed the equation

$$W = A - BR^n \tag{5.3d}$$

or when $A = B$,

$$W = A(1 - R^n) \tag{5.4b}$$

which are evidently similar to our equations (5.3a) and (5.4a), respectively, by letting

$$e^{-k} = R^n$$

R^n, or e^{-k} being the ratio of the successive increments—of the second to the first, third to the second, and so on, which is constant—resulting from the corresponding unit increments of fertilizer, food, or other causative factors. W is the cumulative weight associated with the consumption of n units of food.

5.2: The principle of diminishing increments and the net energy values of cattle and rabbit feeds. The net energy per unit food is the gross energy less the energy losses associated with its utilization (Sect. 2.3). From the law of the minimum, food-value tables notwithstanding, the net energy per unit food is not a constant but varies with many circumstances, such as the balance between nutrients *in relation* to their use in the body, amount of roughage, environmental temperature, endocrine constitution of the animal, and plane of nutrition. Brody and Procter[7] have investigated mathematically, from the viewpoint of the principle of the diminishing increments, the influence of the plane of nutrition, or amount of feed ingestion, on the digestible-, metabolizable- and net-energy values of steer and rabbit rations.

The data were obtained by Forbes *et al.*[10] (Pa.) on 433-kg steers, Mitchell *et al.*[11] (Ill.) on a 613-kg steer, and Wiegner[12] on a 2.8-kg rabbit. The data (interpolated from smoothed curves) are given in Table 5.1 and the fit of equation (5.4) to the relation between net energy to total feed intake is given in Fig. 5.1.

As indicated by the statistical constants, Sy, r, and average deviations, equation (5.4) fits the data excellently.

The average equation for the Pa. (Forbes) steers is

$$Q_n = 24000(1 - e^{-.000025Q_g})$$

which means that the average theoretical maximum net energy obtainable per day is 24000 Cal, and that the net energy, Q_n, rises with the intake of gross energy, Q_g, at decreasing increments; that for every 1000 Cal (about $\frac{1}{2}$ lb feed) increase in gross energy, Q_g, the decline in the net energy rise is about 2.5 per cent.

[10] Forbes, E. B., Braman, W. W., and Kriss, M., *et al.*, *J. Agri. Res.*, **37**, 253 (1928); **40**, 37 (1930); *J. Nut.*, **5**, 183 (1932); **15**, 565 (1938).

[11] Mitchell, H. H., Hamilton, T. S., *et al.*, *J. Agr. Res.*, **45**, 163 (1932).

[12] Wiegner, G., und Ghoneim, A., *Die Tierernährung*, **2**, 193 (1930).

TABLE 5.1. The Relations Between Planes of Nutrition and Gross, Digestible, etc., Energy Intakes; Also the Losses (Feces etc.) at Corresponding Planes.

The Planes of Nutrition Are Represented in Terms of Multiples of the Postabsorptive Heat Production ("Basal Metabolism" or B). Planes 1.0B, 1.5B, and 2.0B Represent Respectively 1.0, 1.5, and 2.0 Times the "Basal Metabolism," and the Corresponding Gross, Digestible etc. Energy Intakes Furnish *Net-Energy* Equivalents to the 1.0, 1.5, and 2.0 Times the "Basal Metabolism." The Numerical Values Given in This Table were Interpolated Carefully from the Curves of the Several Charts.

	Av. of Forbes' Four Steers—Av. Wt. = 433 Kg.								Mitchell's Steer—Av. Wt. 613 Kg.								Wiegner's & Ghoneim's Rabbit SB—Av. Wt. 2.81 Kg.			
	Cal/Day				Cal/Kg/Day				Cal/Day				Cal/Kg/Day				Cal/Day		Cal/Kg/Day	
Plane of Nutrition..	0.5B	1.0B	1.5B	2.0B	0.5B	1.0B	1.5B	2.0B	0.5B	1.0B	1.5B	2.0B	0.5B	1.0B	1.5B	2.0B	0.5B	1.0B	0.5B	1.0B
Gross Energy	7200	15132	26700	42900	16.6	34.9	61.7	99.1	7300	17500	29700	43200	11.9	28.5	48.5	70.5	100	351	35.6	124.9
Digestible Energy	5300	11142	18900	28650	12.2	25.7	43.6	66.2	6100	14100	22350	31200	9.95	23.0	36.5	50.9	72	200	25.6	71.2
Digest. Less Methane E..	4600	9825	16800	25650	10.6	22.7	38.8	59.2	5300	12200	19600	27500	8.65	19.9	32.0	44.9	—	—	—	—
Metabolizable Energy	4250	9136	15750	24100	9.82	21.1	36.4	55.7	5050	11720	19000	26400	8.24	19.1	31.0	43.1	68	176	24.2	62.6
Net Energy	3840	7680	11520	15360	8.87	17.7	26.6	35.5	4760	9520	14280	19040	7.77	15.5	23.3	31.1	65.5	131	23.3	46.6
"Basal Metabolism"	7680	7680	7680	7680	17.7	17.7	17.7	17.7	9520	9520	9520	9520	15.5	15.5	15.5	15.5	131	131	46.6	46.6
Feces Energy	1900	3989	7800	14250	4.39	9.21	18.0	32.9	1200	3400	7350	12000	1.96	5.71	12.0	19.6	28	151	9.96	53.7
Methane Energy	700	1317	2100	3000	1.62	3.04	4.85	6.93	800	1900	2750	3700	1.31	3.10	4.49	6.04	—	—	—	—
Urine Energy	350	689	1050	1550	.81	1.59	2.42	3.58	250	480	600	1100	.41	.783	.98	1.79	10	20.5	3.56	7.3
S.D.A. Energy	320	1460	4320	7120	.74	3.37	9.98	16.4	80	2180	4880	7580	.13	3.56	7.96	12.4	2.5	45	.89	16.4
Storage Energy	−3840	0	+3840	+7680	−8.87	0	8.87	17.7	−4760	0	+4760	+9520	−7.77	0	7.77	15.5	−65.5	0	−23.3	0
Total Heat Production	8000	9140	12000	15800	18.5	21.1	27.7	36.5	9600	11700	14400	17100	15.7	19.1	23.5	27.9	133.5	176	47.5	62.6
	Gms/Day				Gms/Kg/Day				Gms/Day				Gms/Kg/Day				Gms/Kg		Gms/Kg/Day	
Dry Matter Consumption	1650	3366	5950	9600	3.81	7.77	13.7	222	1650	4000	6800	9900	2.69	6.53	11.1	16.2	22	80	7.83	28.5
Nitrogen Consumption	32	68.6	123.5	189	.07	.158	.29	.44	31	73	123	186	.05	.119	.20	.30	.47	1.64	.17	.59
Urinary N Excretion	40	45.8	65	89	.09	.106	.15	.21	(30)	42	65	78	.05	.069	.11	.13	.62	.565	.22	.20
Ratio Net E./Gross E., %...........	53.3	50.8	43.1	35.8	—	—	—	—	65.2	54.4	48.1	44.1	—	—	—	—	65.5	37.3	—	—

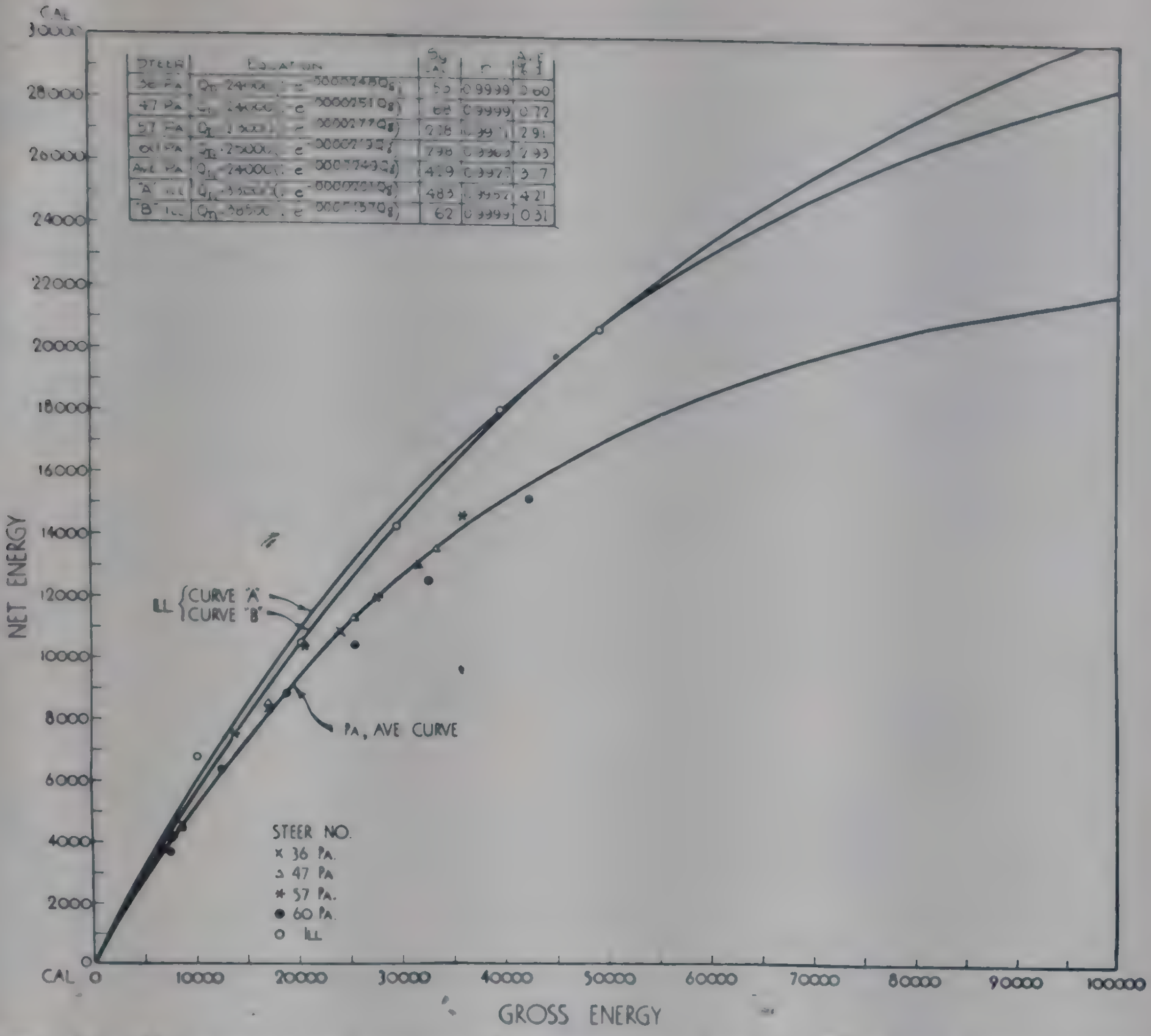

Fig. 5.1—Net energy as function of gross energy intake. The data points represent the observed values; the smooth curves represent the equations given in the upper-left table. In the equations, Q_n represents the net energy, Q_g the gross energy, and e the base of natural logarithms. Curve "A" includes all of Mitchell's data; curve "B" omits the first (1/5-plane) datum. $\pm Sy$ includes 68% of the observed data; r represents the correlation coefficients for the several curves. The table below gives computed values for gross energy (G. E.) and dry matter (D. M.) corresponding to different values of net energy. The values were computed from the equations given in the upper-left table.

Net Energy Cal.	36-Pa. Wt. 479 Kg.		47-Pa. Wt. 484 Kg.		57-Pa. Wt. 398 Kg.		60-Pa. Wt. 369 Kg.		"A"—Ill. Wt. 613 Kg.		"B"—Ill. Wt. 613 Kg.	
	G.E. Cal.	D.M. Kg.	G.E. Cal.	D.M. Kg.	G.E. Cal.	D.M. Kg.	G.E. Cal.	D.M. Kg.	G.E. Cal.	D.M. Kg.	G.E. Cal.	D.M. Kg.
500	847	0.19	837	0.19	794	0.18	913	0.20	796	0.18	828	0.19
1000	1694	0.38	1673	0.37	1588	0.36	1826	0.41	1542	0.35	1656	0.38
1500	2621	0.58	2590	0.57	2419	0.54	2831	0.63	2338	0.53	2548	0.58
2000	3508	0.78	3466	0.77	3285	0.74	3790	0.85	3085	0.70	3376	0.77
2500	4436	0.98	4383	0.97	4152	0.93	4795	1.07	3930	0.89	4268	0.97
3000	5363	1.19	5299	1.17	5018	1.12	5845	1.31	4726	1.08	5159	1.17
3500	6371	1.41	6295	1.39	5957	1.33	6895	1.54	5572	1.27	6051	1.38
4000	7379	1.63	7291	1.61	6895	1.54	7945	1.78	6418	1.46	7006	1.59
4500	8347	1.85	8247	1.83	7870	1.76	9041	2.02	7264	1.65	7898	1.80
5000	9395	2.08	9283	2.05	8845	1.98	10183	2.28	8209	1.87	8853	2.01
6000	11613	2.57	11474	2.54	10903	2.44	12511	2.80	10000	2.27	10764	2.45
7000	13911	3.08	13745	3.04	13069	2.93	14977	3.35	11841	2.69	12803	2.91
8000	16331	3.61	16135	3.57	15451	3.46	17626	3.94	13781	3.14	14841	3.38
9000	18952	4.19	18725	4.14	17906	4.01	20365	4.56	15871	3.61	16943	3.85
10000	21774	4.82	21514	4.76	20614	4.61	23333	5.22	17960	4.09	19172	4.36
12000	27944	6.18	27610	6.11	26643	5.96	29863	6.68	22537	5.13	23822	5.42
14000	35282	7.81	34860	7.72	33849	7.59	37489	8.39	27463	6.25	28790	6.55
16000	44315	9.81	43785	9.69	42996	9.62	46667	10.44	33035	7.52	34267	7.80
18000	55887	12.37	55219	12.22	55082	12.35	58128	13.01	39154	8.91	40191	9.14
20000	72177	15.97	71315	15.78	73646	16.48	73516	16.45	46318	10.54	46624	10.61
22000	100322	22.20	99123	21.94	113357	25.37	96803	21.66	54726	12.45	53885	12.26

Fig. 5.1 is supplemented by the several additional charts, explained below.

Figs. 5.2 A and B represent the net energy as function of intake of (1) gross, (2) digestible, and (3) metabolizable energy, with their equations; Figs. 5.2 a and b represent the ratios of net energy to each: (1) gross, (2) digestible, and (3) metabolizable-energy intake.

Fig. 5.3, plotted on arithlog paper, represents the various losses associated with feed utilization as percentage of the gross energy ingested. The greatest increase in energy loss with increasing plane of nutrition appears to be due to the *SDA*. It rises from about 3 per cent on the 0.5-maintenance ration to about 20 per cent on the 3-maintenance ration.

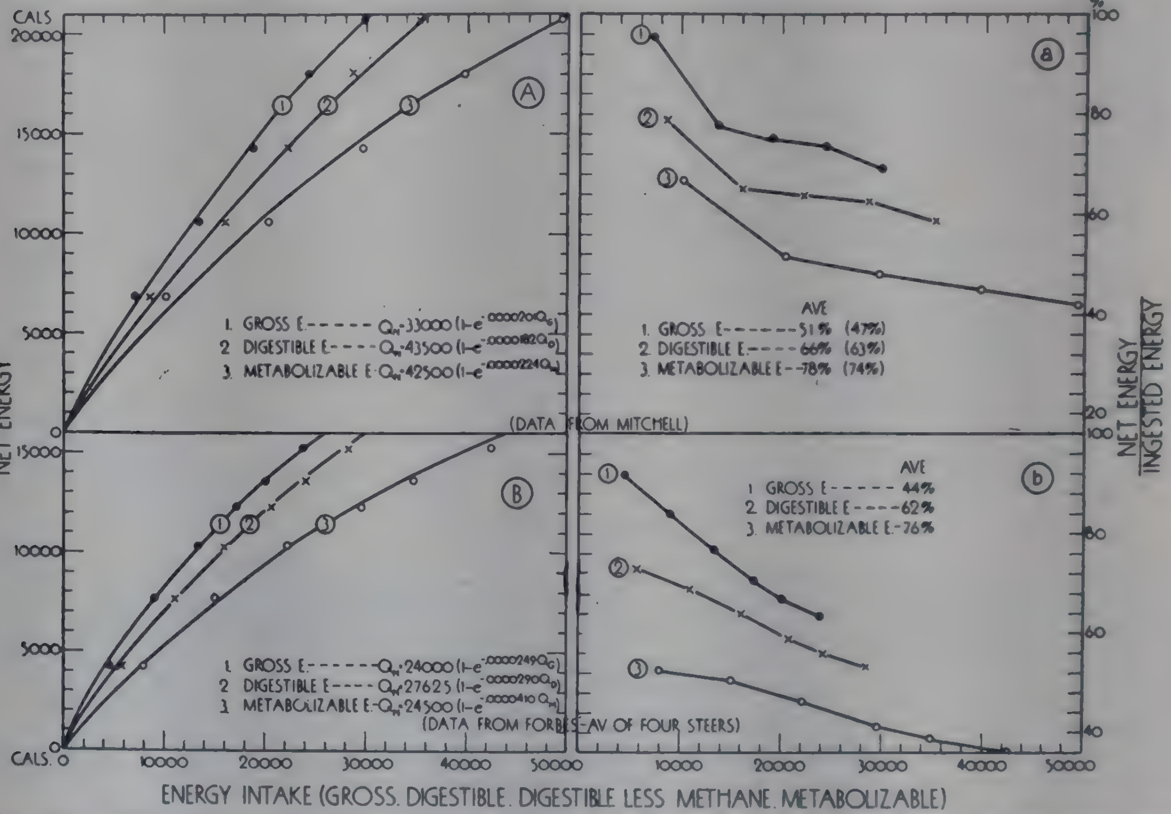

Fig. 5.2—Net energy as function of gross, digestible, digestible less methane, and metabolizable energy. Curves A and B represent respectively Mitchell's and Forbes' (average) steer data; curves a and b represent the percentage ratios of net energy to gross, digestible, digestible less methane, and metabolizable energy for Mitchell's and Forbes' steers. In curves a, the values in parentheses represent the ratios with the 1/5-plane omitted.

The absolute loss is greatest for the fecal energy, but the range in loss is only from 26 to 32 per cent. Even fasting animals pass considerable fecal material, since undigested feed constitutes but a part of the feces.

The methane percentage loss in steers is relatively constant, about 9 per cent of the gross energy. The urinary percentage loss, of course, depends on the nitrogen intake. In this case it ranged from 3 to 5 per cent.

The net energy percentage (of the gross-energy intake) declines for Forbes' steers from about 54 per cent at 0.5 maintenance to about 40 per cent at full

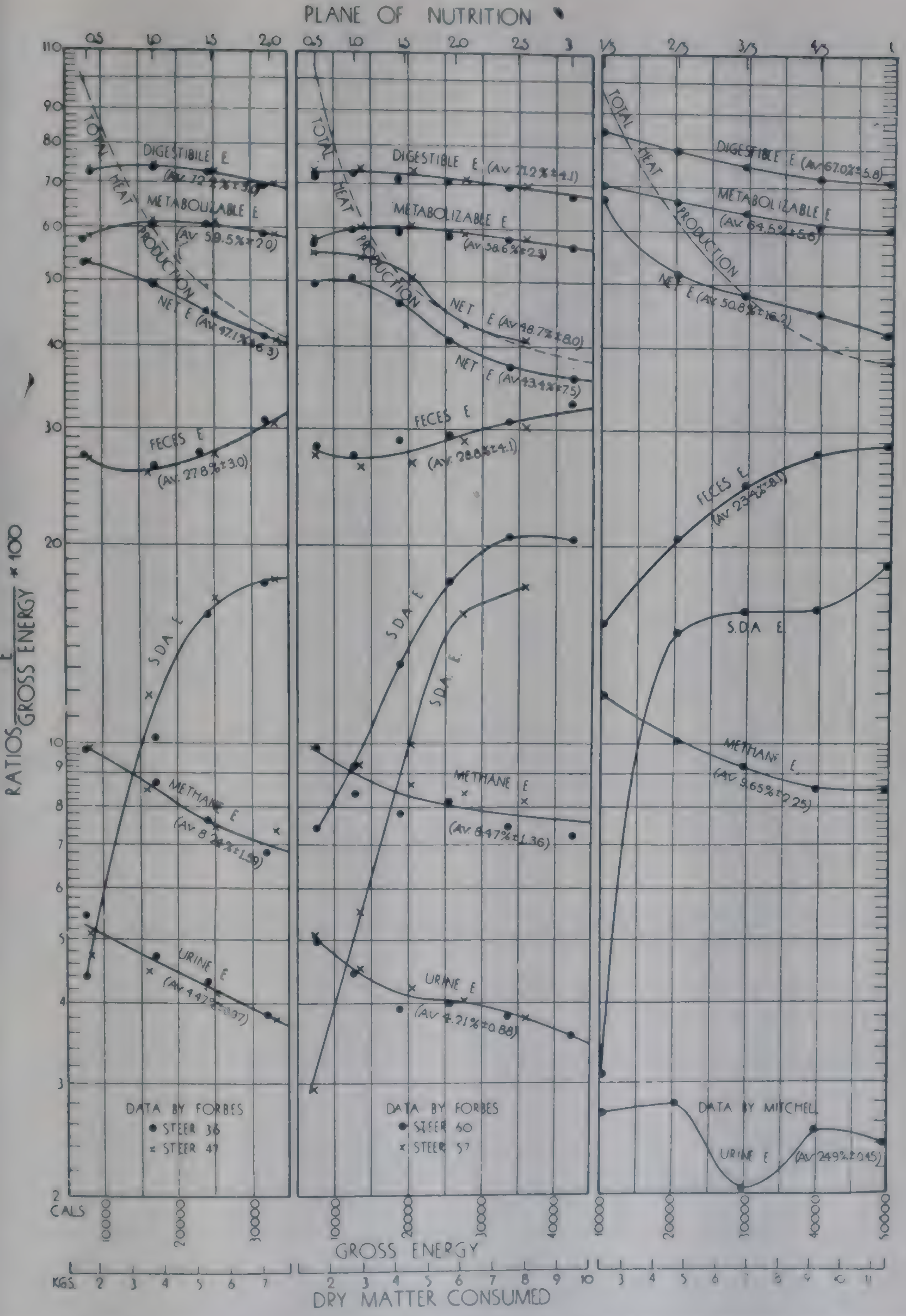

Fig. 5.3—The several losses (urine, methane, S.D.A., and feces) expressed as percentages of gross energy intake; also the net, metablizable, and digestible energies expressed in terms of percentages of gross-energy intake; also, total heat production in terms of percentage of gross energy intake. The planes of nutrition (upper axis) are represented in the case of Forbes' steers in terms of gross energy at maintenance; in the case of Mitchell's steers they are expressed in terms of gross energy at "full feed."

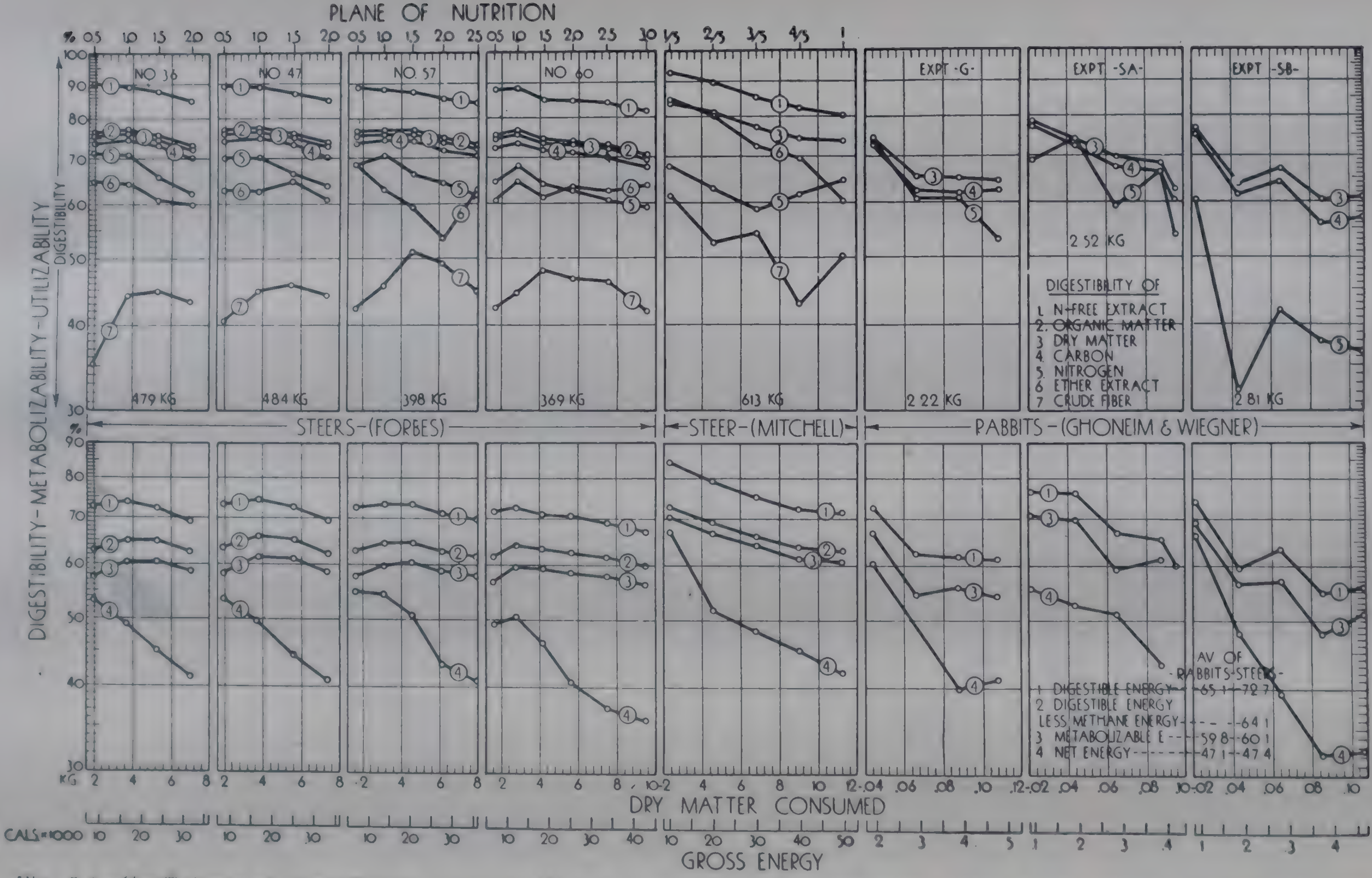

Fig. 5.4—Coefficients of digestibility (upper half) and percentages of gross energy intake as digestible energy, digestible energy less methane energy, metabolizable energy, and net energy (lower half), plotted as functions of dietary gross energy and dry matter in steers and rabbits. The planes of nutrition (upper axis) are represented, in the case of Forbes' steers, in terms of gross energy at maintenance; in the case of Mitchell's steer, in terms of

eed, and for Mitchell's from about 65 to about 42 per cent. The declines in ligestibility and metabolizability with increasing plane of nutrition are less conspicuous.

The other charts and tables call for less explanation. The upper segment in Fig. 5.4 presents the course of digestibility of the several dietary constituents with increasing plane of nutrition; the lower segment, the course of the percentage changes of the various energy categories with increasing plane of nutrition.

Fig. 5.5 presents the ratios of net energy to digestible energy plotted against plane of (1) gross energy intake, (2) digestible energy, and (3) basal energy.

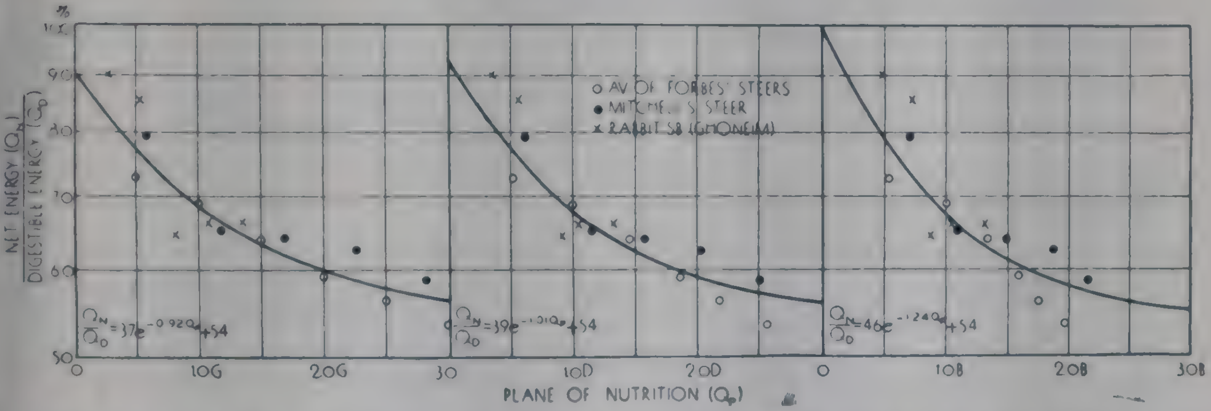

Fig. 5.5—Ratios of net energy to digestible energy of the steer and rabbit data plotted against planes of net nutrition expressed in terms of 1, 2, etc., times gross energy intake (1G, 2G, etc.); digestible energy (1D, 2D, etc.), and "basal" energy (1B, 2B, etc.) intake with the corresponding equations. The data are plotted on arithlog paper. Note that the rabbit and steer data nearly coincide.

The equation of the ratio of net energy, Q_n, to digestible energy, Q_d, plotted against the plane of nutrition, Q_p, is

$$Q_n/Q_d = 43e^{-Q_p} + 54$$

indicating that the net energy does not fall below 54 per cent of the digestible energy.

Finally, Fig. 5.6 represents the influence of the plane of nutrition on (1) various energy losses; (2) various feed-energy categories; (3) body loss or storage for the three groups of animals. The gains or losses at any point of food ingestion are shown by the lengths of the ordinates at the given point between the indicated limits. Note that at the maintenance-balance level, the net energy value is identical with the basal-metabolism value, and the total heat production curve crosses the metabolizable-energy curve.

In summary, increasing food intake tends to reduce the net-energy value per unit food in accordance with the principle of diminishing returns. A detailed analysis is presented on the applicability of the principle to the

course of net-energy change of cattle and rabbit feeds with increasing plane
nutrition as observed on 430-kg and 615-kg steers and on a 2.8-kg rabbit.

5.3: The principle of diminishing increments and food consumption durin growth. We have seen (Sect. 3.2.3) that as the animal grows larger, its main

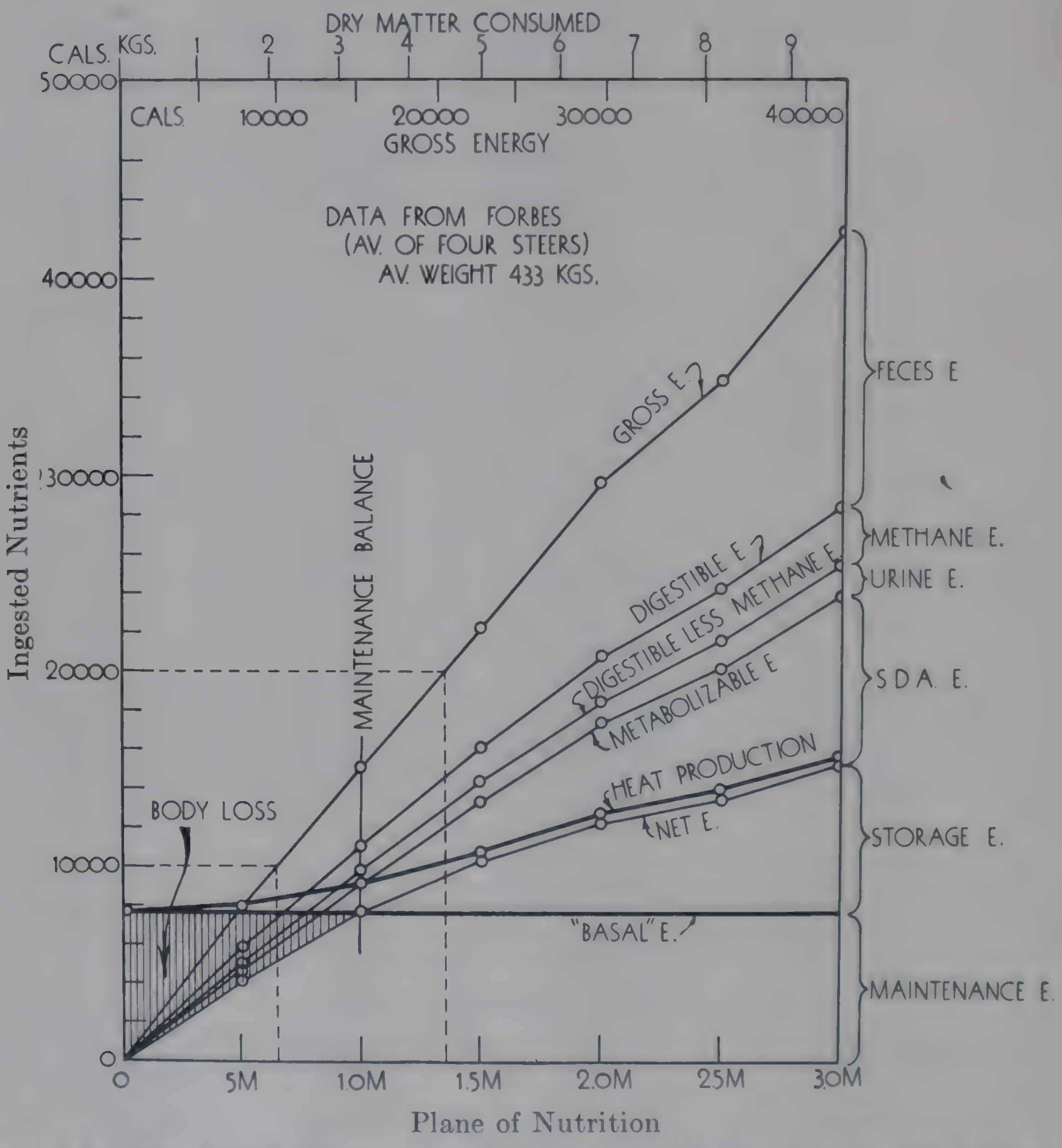

Fig. 5.6a—The relations between the plane of nutrition and the energy losses in the forms of feces, methane, urine, SDA in cattle; also energy storage (fattening) following the maintenance level, and body losses preceding the maintenance level. The gains or losses at any point of food ingestion are determined by the lengths of the ordinates at the given point between the indicated limits. At the maintenance level the net-energy curve crosses the "basal" metabolism curve, and the metabolizable-energy curve crosses the total heat production (basal plus *SDA* energy) curve.

tenance cost in comparison to weight gain increases and, therefore, the energetic efficiency of growth decreases; that is, as the animal approaches mature weight, the successive increments in body weight decrease per unit food intake; finally, growth virtually ceases while food consumption continues for maintenance alone.

Spillman[3] and more recently Jull, Titus, and Hendricks[8] applied the exponential, or diminishing-increment, equation relating growth to feed consumption in farm animals. Equation (5.4) represents very satisfactorily the interrelation between weight and feed consumption *during growth*. It is evident that while the general principle is the same, the causative factors are of different nature for the effect of food-intake level on growth when age and

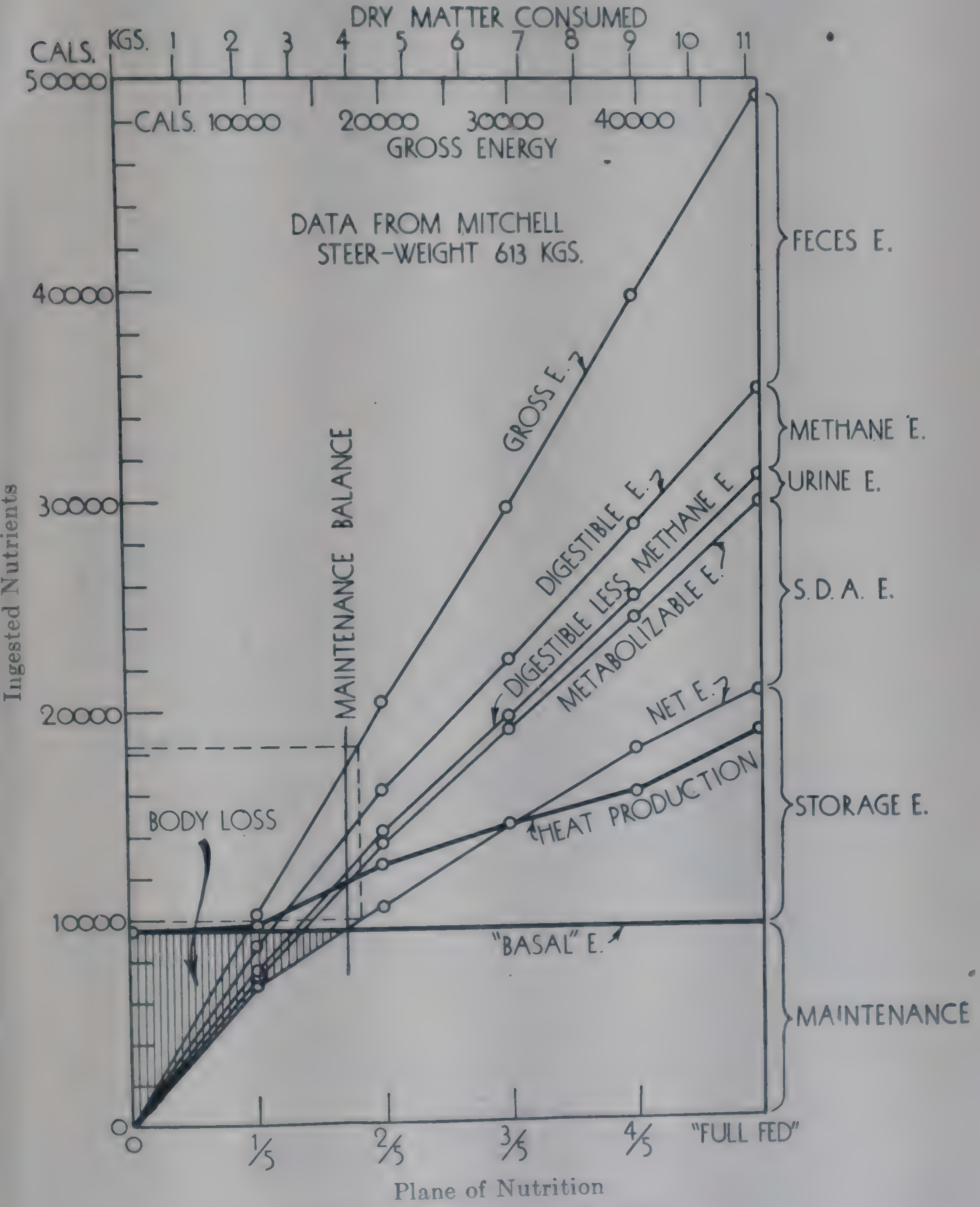

Fig. 5.6b—Same legend as 5.6a.

body weight are increasing than for the effect of food-intake level on the net energy at a constant age discussed in the preceding section.

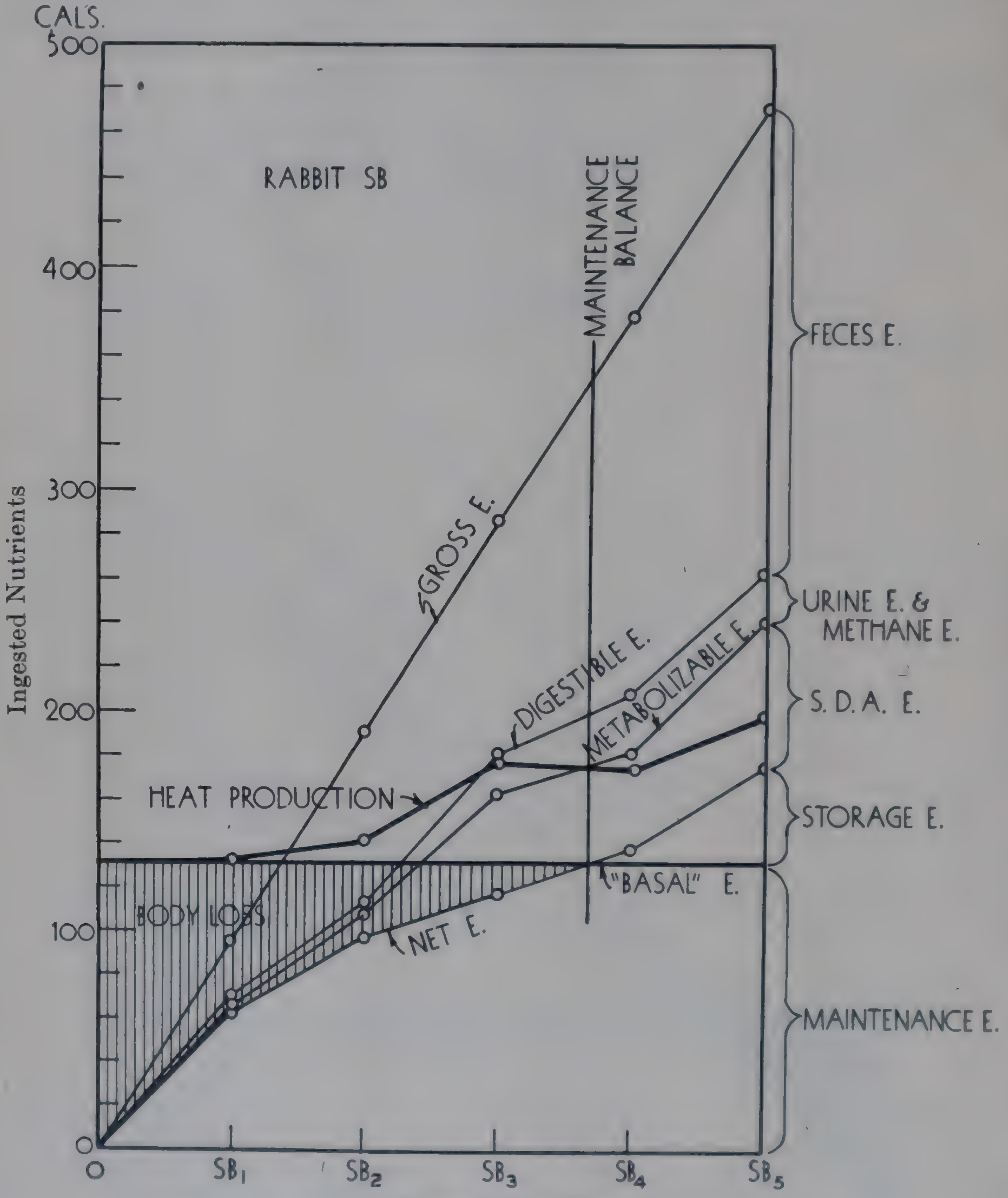

Fig. 5.6c—A continuation of Fig. 5.6a, as it relates to the rabbit.

Fig. 5.7 is offered as an illustration of the relation of body weight to the total feed consumption with increasing age in immature chickens. The given equation indicates that the differential successive weight gains per kilogram feed consumed decline at the rate of 9 per cent; that is, each weight-gain increment per kilo feed consumed is roughly 9 per cent less than the preceding increment;

or what is the same, each increment is roughly 91 per cent of the preceding increment. The value 3.7 represents the theoretical maximal body weight in kg attainable by these chickens.

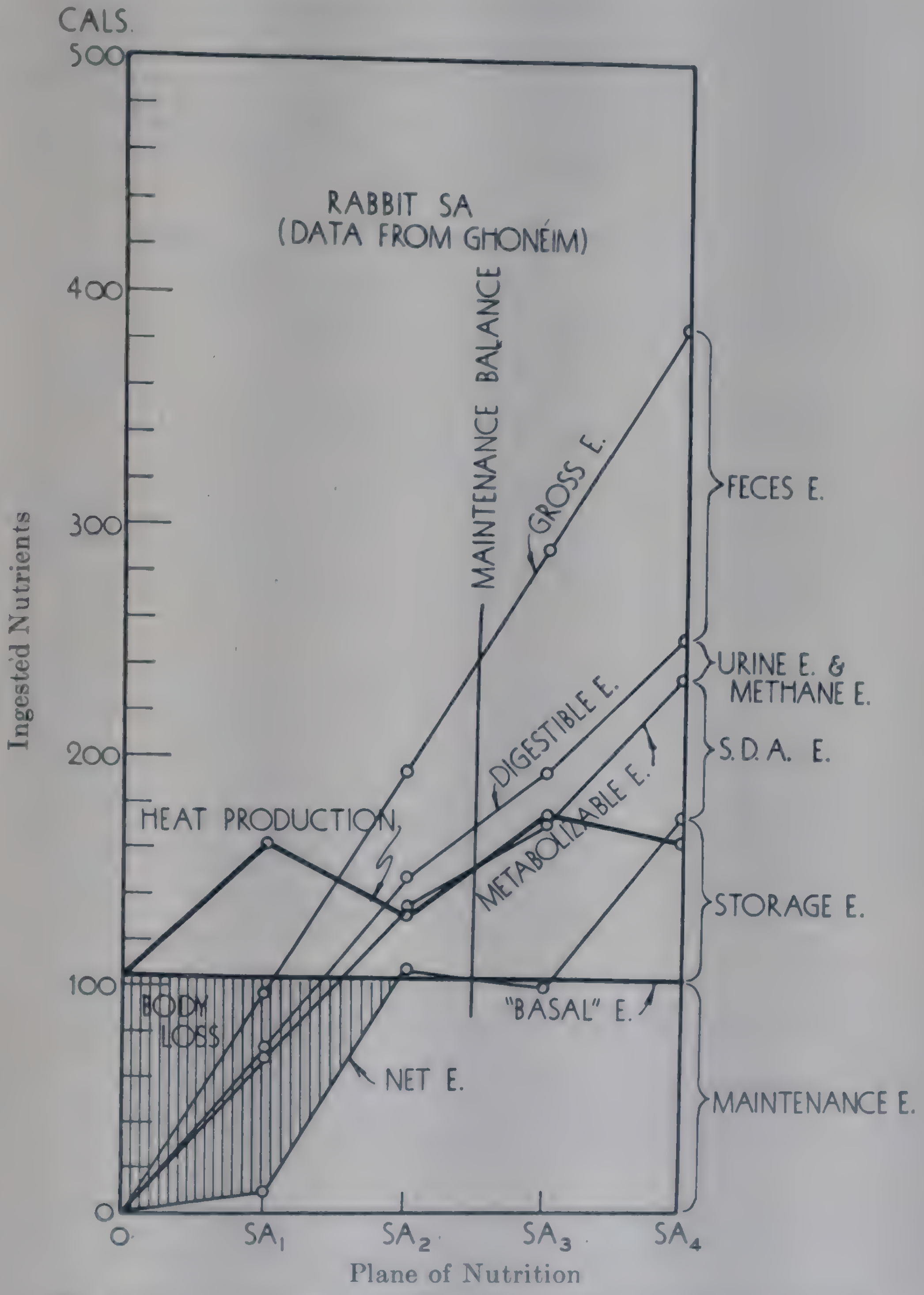

Fig. 5.6d—A continuation of Fig. 5.6a, as it relates to the rabbit.

For additional illustrations of the application of equations (5.3) and (5.4) to the interrelations between growth and feed consumption, the reader is referred to the literature cited and to the preceding chapter (Sect. 3.2.3) which contains data suitable for analysis from this viewpoint.

The foregoing discussion was concerned with the interrelations between weight gains and "normal" food consumption associated with *advancing age* during growth, regardless of the efficiency or economy aspect. We also have the problem of influence of rate of weight gains and of plane of nutrition on feed economy (in contrast to *total* economy including cost of labor, etc.). Is it more economical to feed, for example, growing pigs *ad libitum* or to restrict to lower levels? It is usually assumed that the greater the feed consumption the more rapid the growth and the more economical the gains because of the saving of some maintenance cost per unit weight gain. On the other hand, as previously noted, the greater the feed intake the lower the feed utilization, and the less the net energy per unit feed consumption. Moreover, underfed animals develop a "growth debt" which may enable them to utilize food more efficiently than well-fed animals.

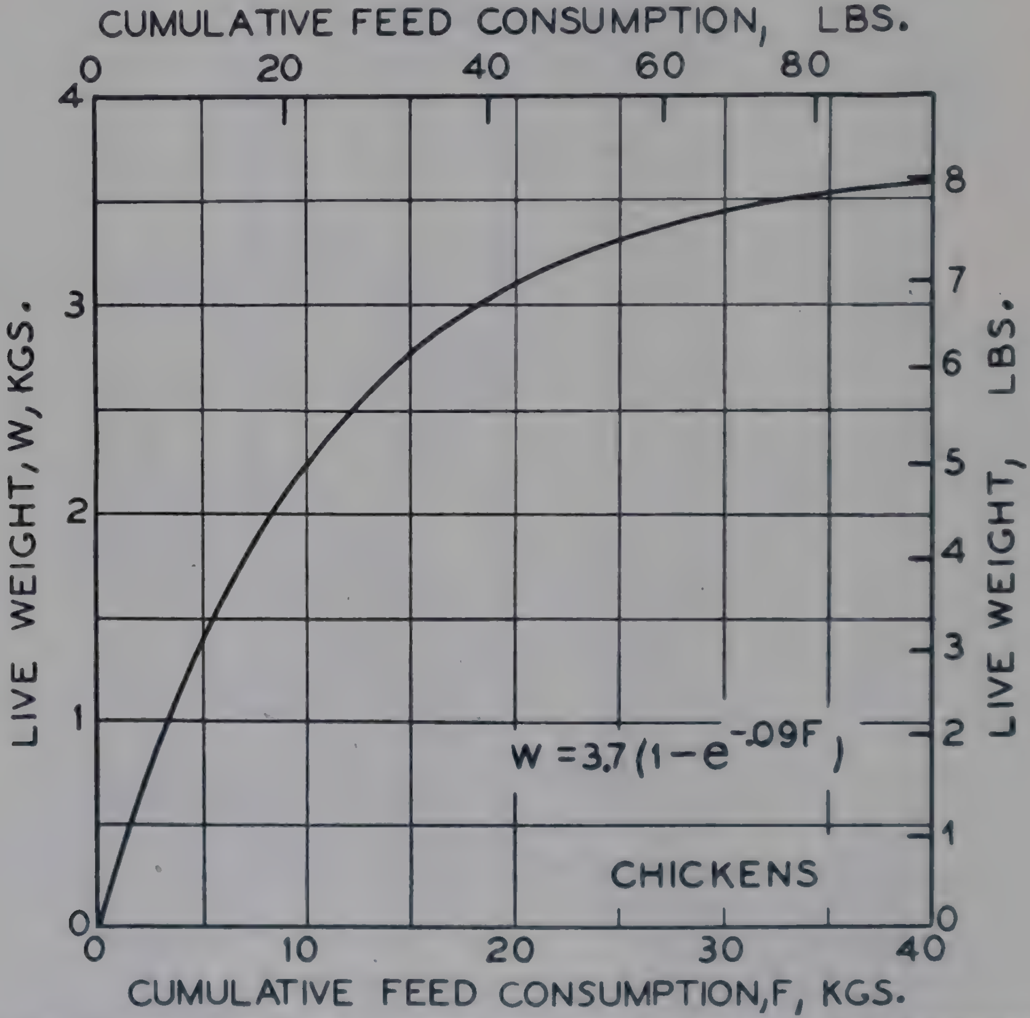

Fig. 5.7—The relation between live weight and cumulative feed consumption in growing chickens.

Considerable research has been conducted at the Missouri Station[13] on the growth of cattle on various planes of nutrition (Ch. 16). At this time reference is confined to the results of Ellis and Zeller[14] on the feed required to increase the body weights of pigs by 50 pounds, from an initial 70 to a final 120-pound level, when the pigs are fed *ad libitum*, at 4, 3, and 2 pounds feed per 100 pounds body weight. It was observed that while the growth rate decreased with decreasing feed allowance, the weight gain per unit feed consumed increased: one pound feed yielded 0.24, 0.29, and 0.32 pound of body weight gain when the animals were fed, respectively, 4, 3, and 2 pounds feed per 100 pounds live weight. The lowest plane of nutrition required 40 per cent more time to make a given gain in weight, yet yielded 33 per cent more body weight per unit feed. These differences in weight gains are, however, not indices of differences in gross *energetic* growth efficiency because the gains in the slowly growing animals contained more lean and water and less fat tissue than in the rapidly growing: the body fat constituted 36, 34, and 29 per cent respectively on the 4-, 3-, and 2-pound planes of nutrition.

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[13] Missouri Agric. Exp. Sta. Res. Bulls. 43, 54, 55, and others.

[14] Ellis, N. R., and Zeller, J. H., U.S.D. Agriculture, Tech. Bull. 413, 1934.

5.4: The principle of diminishing increments and milk production. We shall discuss two types of diminishing increments in milk production: (1) that of energetic efficiency with increasing milk production level associated with inherent differences in lactational capacity on a standard ration, and (2) milk yield with increasing feed consumption in the same animals in which feed consumption is deliberately controlled by adding more or less of grain to the ration.

The diminishing-increment course of gross energetic efficiency of milk production with increasing milk yield is indicated in Figure 1.2 (page 5). The causal factor actuating the decline in increments is evident. The *gross* energetic efficiency, which carries the maintenance burden, can never be as great as the *net* efficiency, which is not thus burdened with the maintenance tax. With increasing milk yield the gross efficiency approaches the net efficiency as a limit. From its asymptotic nature, this approach occurs at ever-decreasing increments.

The causal mechanism actuating the decline in milk increments with successive units of grain intake in the same animal is of a more complex nature. There is first the decline in feed utilization, in net energy per unit feed with increasing feed intake (Sect. 5.2). Secondly, there may be a decline in the energetic efficiency of the entire milk-producing mechanism with increasing lactation rate above a certain production level similar, for example, to the decline in the energetic efficiency of an automobile with increasing driving speed above about 30 miles an hour (Ch. 24). Table 5.2 appears to indicate that the gross energetic efficiency of milk production tends to decline if increased milk production is brought about by feeding beyond certain levels.

The *gross* energetic efficiency of milk production may be estimated (Ch. 21) by dividing the Calorie equivalents of the milk yield (pound $FCM \times 340$) by the Calorie equivalent of the feed consumed (pounds $TDN \times 1814$). The *net* energetic efficiency of milk production may be similarly estimated by dividing the Calorie equivalent of the milk yield by the Calorie equivalent of the feed consumed *above the maintenance level.* There is, of course, a large error in estimating maintenance—distinct from production—of a producing animal, and for this reason the *net* energetic efficiency of milk secretion is less close to reality than is the gross efficiency.

TABLE 5.2. Milk Production as a Function of *TDN* and Grain Consumption.

Feeding level % of Haecker's standard above total maintenence		*TDN* consumed million Cal	*TDN* consumed above maintenance million Cal.	Milk produced million Cal.	Energetic efficiency of milk products	
					gross (%)	net (%)
96	91	10.256	4.256	2.593	25.3	60.4
101	102	11.096	5.132	2.783	25.1	54.2
105	110	11.931	5.963	3.000	25.1	50.3
110	120	12.937	6.973	3.196	24.7	45.8
114	128	13.661	7.697	3.325	24.3	43.2
116	138	14.329	8.364	3.388	23.7	40.5

The above values were computed from the following data by Jensen *et al.*[9]

Feeding level % of Haecker's standard above total maintenence		No. lactations	*TDN* consumed (lbs)	*TDN* consumed above maintenence (lbs)	Milk (*FCM*) produced (lbs)	Grain consumed (lbs)
96	91	65	5654	2366	7626	1722
101	102	60	6117	2829	8184	2098
105	110	66	6577	3287	8824	2777
110	120	55	7132	3844	9400	3666
114	128	52	7531	4243	9780	4132
116	138	94	7899	4611	9965	5304

The following data are from Borland.[15]

Feeding level (% of Haecker's standard)	No. records	Grain consumed (lbs)	Milk (*FCM*) produced (lbs)	Milk (*FCM*) per lb grain	Feed cost per cow (dollars)	Feed cost per lb milk (cents)	Value of milk over feed cost per cow (dollars)	Feed cost per cow (dollars)	Feed cost per lb milk (cents)	Value of mi'k over feed cost per cow (dollars)
70	2	1511	7993	5.3	95.03	1.19	112.79	90.91	1.14	148.88
80	10	2248	8816	3.9	107.30	1.22	121.92	100.95	1.15	163.53
90	9	3455	10253	3.0	119.07	1.16	147.51	110.12	1.08	197.47
100	9	4221	11518	2.7	148.44	1.29	151.03	136.08	1.18	209.46
110	10	4751	10879	2.5	150.66	1.39	132.19	136.61	1.26	189.76
120	4	6221	12170	2.0	174.04	1.43	142.37	155.64	1.28	209.46
123	22	7300	12756	1.75	191.60	1.43	140.06	164.80	1.29	217.88
					Grain costs 1.8¢ per lb Milk sells for 2.6¢ per lb			Grain costs 1.5¢ per lb Milk sells for 3¢ per lb		

The gross and net energetic efficiencies of milk production as function of plane of nutrition in Table 5.2 were estimated from the previously cited report by Jensen and associates.[9] The increase in *TDN* consumption was attained by increasing the grain allowance; the roughage was fed *ad libitum* in all cases.

Jensen's original summary, from which the efficiency estimates were made, is also listed in Table 5.2. Following Jensen's summary table are listed similar data by Borland[15] and associates in which, however, not the TDN consumed, but only grain supplement consumed is given. As previously noted, the increased TDN consumption is achieved by increasing the grain allowance, the animals being always allowed all the roughage they will consume. Borland's data include milk produced per pound grain offered, and the money values involved. While the milk return per pound grain decreases with increasing grain offerings, the profits per cow—and, therefore, per herd—increase with increasing grain feeding, that is, when the cost of grain and return for milk are as here given. The profits, of course, vary with the relative market prices of milk and grain. The higher the milk price and the lower the grain cost, the greater the profit on increased grain feeding. If the expenses of housing, labor, and management were taken into consideration, the higher grain levels would show higher profits (Ch. 22). Since the feed (and bedding) item constitutes only about 50 per cent of the cost of milk production, the remaining 50 per cent of the cost goes for labor (about 30 per cent) and other expenses (20 per cent); and the labor and other overhead expenses are virtually the same for high and low-milking cows. It is possible, however, that the high feeding level may have an unfavorable long-range effect, such as development of mastitis and, in general, acceleration of the senescence process (Ch. 18), analogous to the unfavorable effect of overworking a horse, or driving machinery above certain speeds. Paraphrasing Jensen, it is easy to obtain large crop yields by the lavish use of fertilizer, but does it pay, both this year and in the long run? The time and economic elements complicate all the conclusions.

The above summaries demonstrate that increased TDN consumption, brought about by increased grain allowance, tends to increase the milk yield, but at decreasing increments with successive feed units in accordance with the principle of diminishing increments. Jensen fitted the Spillman diminishing-returns equation $W = A(A - R^n)$ to these data, as shown in Fig. 5.8. The satisfactory fit of this equation does not prove anything, since the range of the data is so narrow that a linear or parabolic equation would probably fit equally well. The theory and, therefore, the fitting of the equation of the principle of diminishing increments to these data is, however, reasonable.

An important feature of Jensen's data is the difference in response of "good" and "poor" cows to increased grain allowances, as illustrated by Fig. 5.9. This, of course, is what might be expected: high milk production is not only the result of high feed consumption but also of the ability or the competence of the cow to convert the extra feed into milk.

The following table from Borland is cited by way of simple summary of the discussion of diminishing milk increments with increasing grain allowance.

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[15] Borland, A. A., Bean, A. L., and Jones, P. D., "The relation of grain feeding to milk production", Pennsylvania Agric. Exp. Sta. Bull. 424. 1942.

Grain fed % of Haecker's standard (%)	Milk (*FCM*) yield per lb of grain fed (in addition to *ad libitum* roughage, etc.) (lbs)
90	1.4
100	1.1
110	1.0
120	0.8
130	0.6

It may be noted[16] that dairy animals produce about 80 per cent as much milk energy on an exclusive, good, roughage ration as on a roughage ration supplemented with about 1 lb grain per 6 lb milk (*FCM*), and that it generally pays to feed at least 1 lb grain to 5–6 lbs milk.

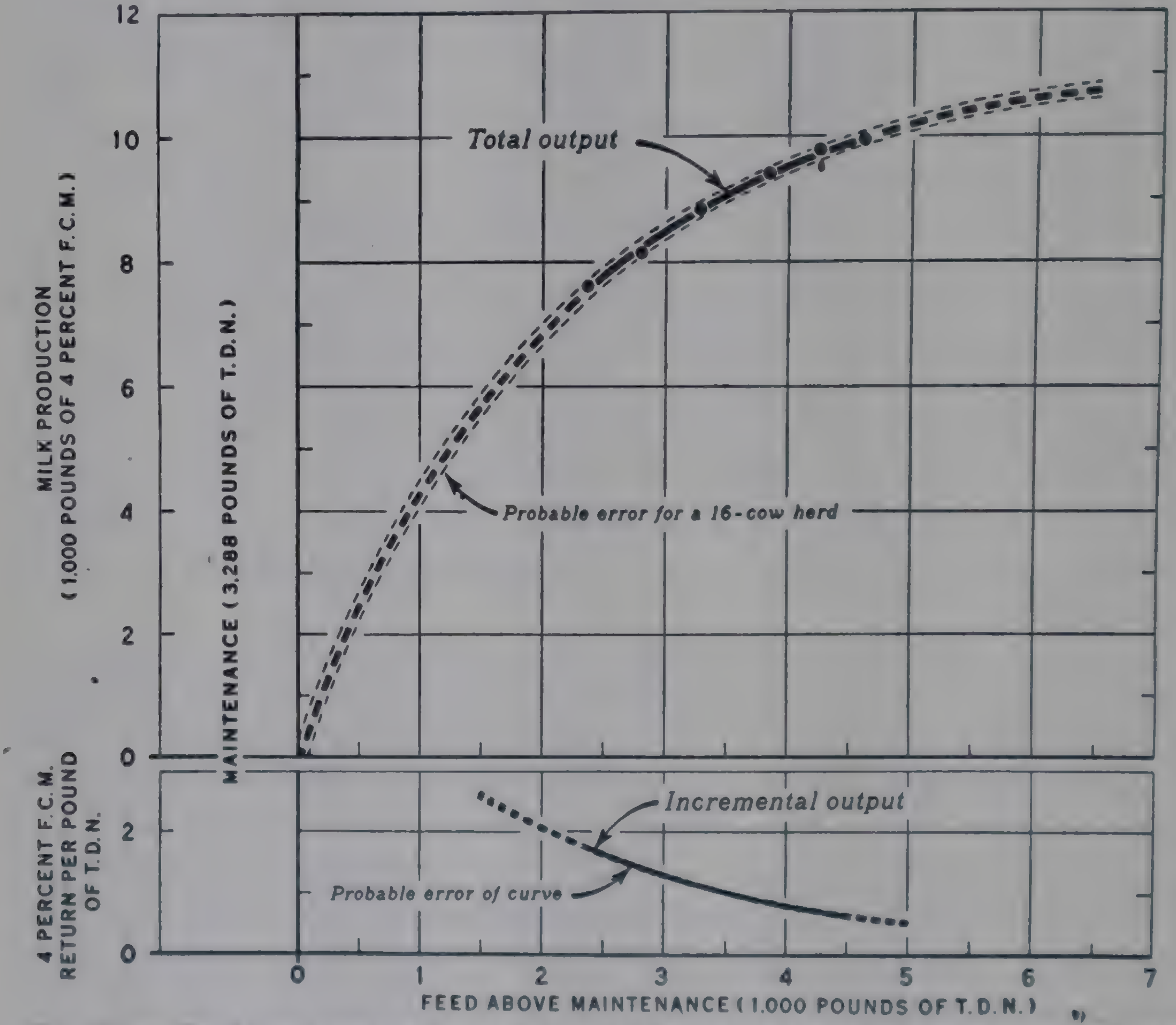

Fig. 5.8a—Feed input and milk output of all cows fed at six different levels of feeding at nine stations conducting experiments in series I and II.

Why is an *ad libitum* roughage ration inferior to a roughage *and* grain ration? Probably because of physical limitations in handling sufficient roughage to supply the needed net nutrients for a high level of milk production, since one pound of grain is equivalent in net energy to several pounds of roughage. Hence the greater the lactational capacity of the cow, the greater should be the ratio of grain to roughage. It is, moreover, probable that a pound of *TDN* in the form of grain has a higher nutritive value than it has in the form of roughage. In other words, roughages may be over valued when represented in terms of the conventional *TDN* (Sect. 2.3).

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[16] *Cf.* Jensen[9]; Borland[15]; Woodward, T., E., Shepherd, J. B. and Graves, R. R., Report U.S.D. Agr. Misc. Publ. 179, 1933. Sherwood, D. H., and Dean, H. K., "Feeding alfalfa hay alone and with concentrates", Oregon Agr. Exp. Sta. Bull. 380, 1940. Headley, F. B., "Economics of feeding hay and grain to cows", Nev. Agr. Exp. Sta. Bull. 140, 1935. Graves, R. R., *et al.*, "Milk production on four plane of feeding U.S.D. Agr. Tech. Bull. 724, 1940.

The general conclusion follows that the greater the lactational capacity of the cow the greater the effect of the grain supplement on milk production (Fig. 5.9). This is an illustration of a broad principle: good environment is good only in relation to the organism's ability to benefit thereby (Ch. 10).

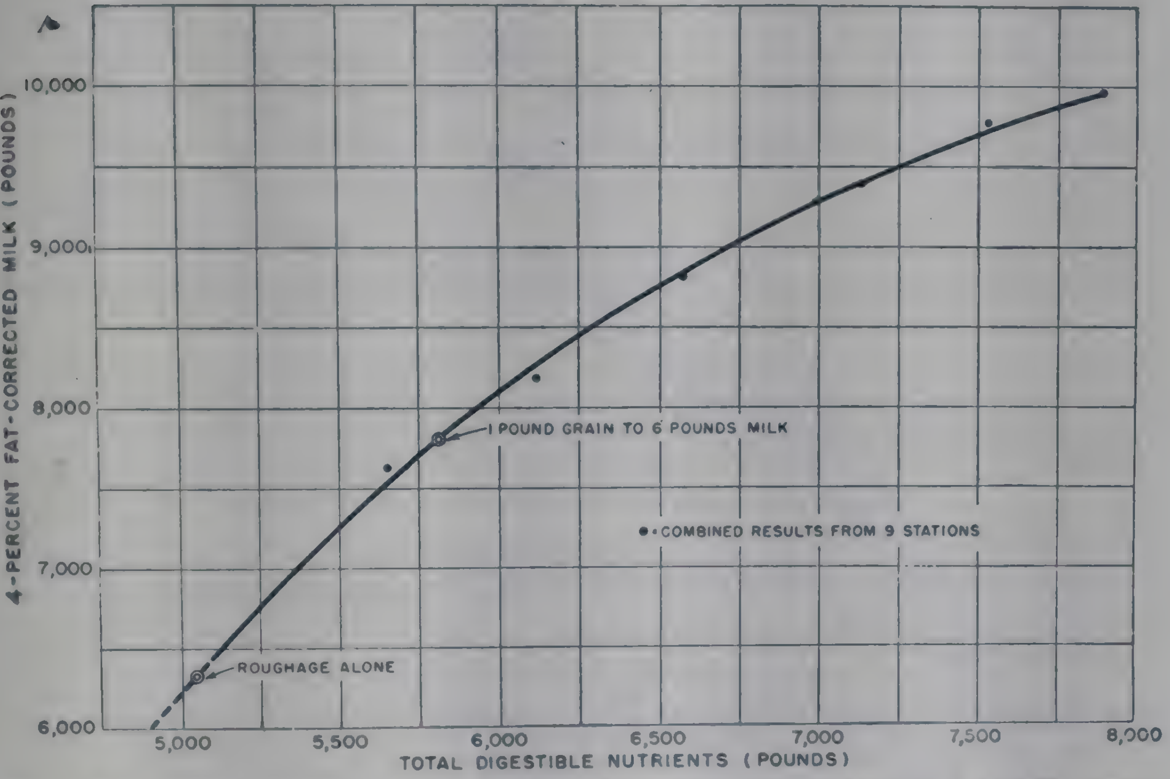

Fig. 5.8b –Chart, based on the smoother data of experiment series I and II combined, and roughage alone of series II, nonpasture stations after adjustment of series II data for difference in basic producing ability of the cows.

5.5: The principle of diminishing increments and egg production efficiency. Fig. 1.1 (page 3) indicates that the gross efficiency of egg production increases at diminishing increments with increasing egg-production level associated with inherent differences in production capacity. The mechanism of this relation is similar to that of increasing gross efficiency of milk production at diminishing increments associated with inherent differences in lactational capacity, explained in the preceding section.

While no data are available, there is no doubt that egg production is related exponentially to feed consumption in the same manner that milk production is associated with feed consumption, that is, in accord with the principle of diminishing increments.

5.6: The principle of diminishing increments and muscular-work efficiency. Figs. 1.3 and 1.4 (p. 7 and 9) and many charts in Ch. 24 indicate that the gross efficiency of muscular work increases with increasing work rate, but at diminishing increments, in the same manner as the gross efficiency of milk or egg production increases with increasing productive level and for the same reason: the greater the speed of work the less the maintenance cost per unit product, approaching net efficiency (not including maintenance) as limit.

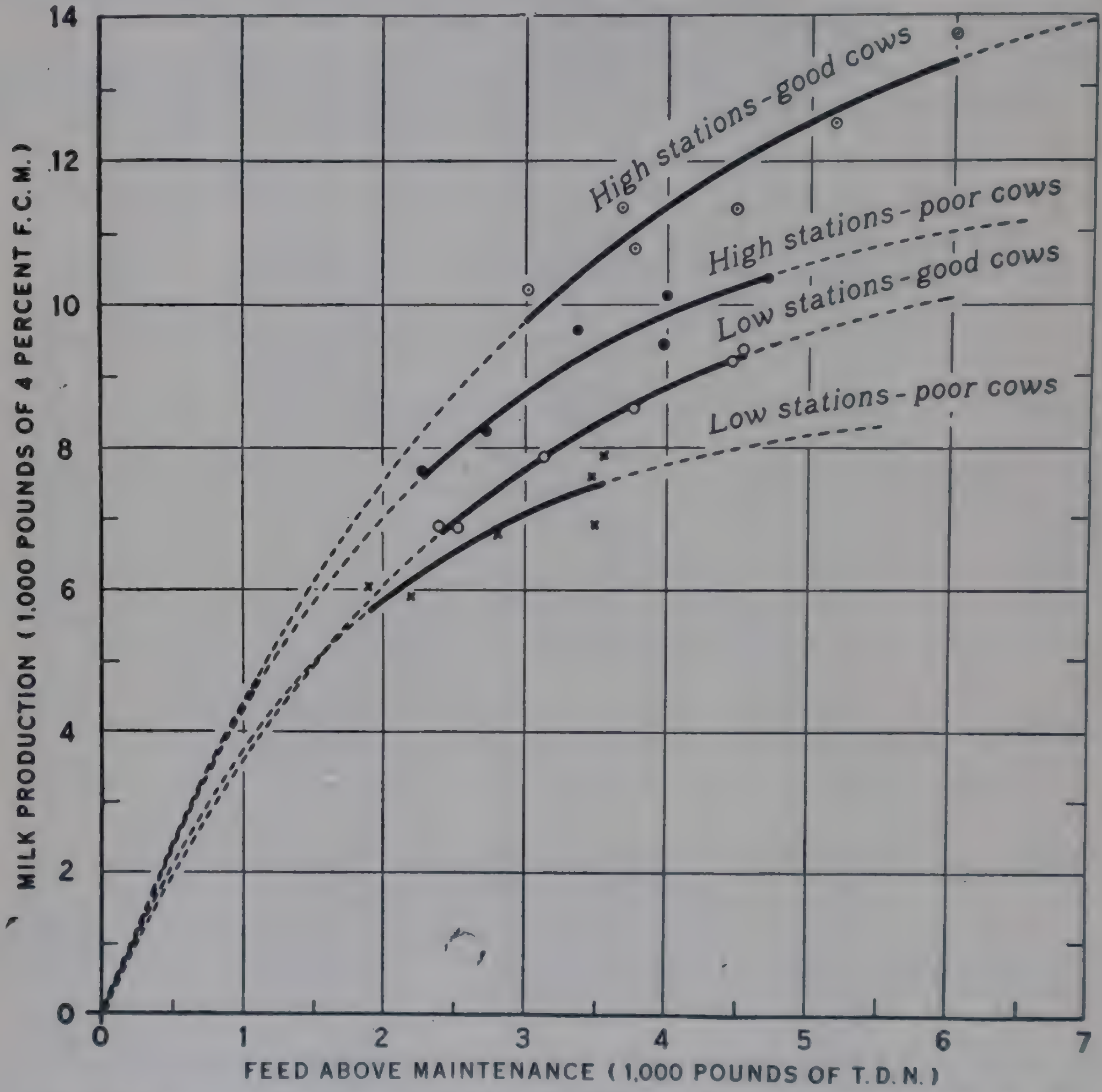

Fig. 5.9—Input-output curves of cows of different inherent productivity at the nine experiment stations.

The fact that the gross efficiency of muscular work increases with increasing rate of work does not mean that it is desirable to work at a high rate; increasing the rate of work beyond a reasonable level tends to injure the animal and shorten its productive life. There is, above a certain productive level, an incompatibility between immediate and long-range efficiency. The same appears to be true of other productive processes such as milk and egg production; the span of the productive life is an important element in the overall production and profit pictures.

5.7: Summary and appendix. This chapter discusses the common-sense and mathematical aspects of the very broad principle of diminishing increments. This principle is illustrated in detail by the influence of the plane of nutrition on digestibility, metabolizability, and especially on the net energy values of rations. Increasing the plane of nutrition (above the maintenance level) increases the losses per unit feed, and therefore decreases the net energy per unit feed. In other words, the net-energy intake increases less rapidly than the gross-energy intake, in accordance with the principle of diminishing increments (Fig. 5.1).

The net energy value per unit feed is thus not constant but varies with the plane of nutrition and with many other factors. Armsby's published net energy values[17] do not, therefore, have the constant significance that they were originally given. Armsby (like Kellner) assumed a direct proportionality between net energy and gross energy consumption, an assumption contrary to the principle of diminishing increments.*

For practical purposes, however, it is legitimate to assume average values. We conclude from the analysis of the data that the average cattle ration employed, which had a combustion value of 2000 Cal/lb (4.5 Cal/g) had an average apparent digestible-energy value of about 1600 Cal/lb (3.2 Cal/g) of the original feed, a metabolizable energy of 1200 Cal/lb (2.7 Cal/g) of the original feed and a net-energy value of about 1000 Cal/lb (2.2 Cal/g) of the original feed (see lower table in Sect. 2.6). The *approximate* apparent digestible energy of the given feed is thus about 70 per cent of the gross energy; the *approximate* metabolizable energy of the given feed is about 60 per cent of the gross energy, and the *approximate* net energy value of the given cattle ration is about 50 per cent of the gross energy. The *exact* values, however, vary with the plane of nutrition and many other factors discussed in the text (Table 5.1 and Figs. 5.3 and 5.4).

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* Illustration of Armsby's direct-proportionality or linear method for computing the heat increment of feeding, the fasting heat production, and the net energy of feeds:

Period	Dry matter in feed (kg)	Heat production (Cal)	Heat increment (Cal/kg dry matter)	Extrapolated fasting maintenance (Cal.)
1	3.6674	8224	706	5635
2	5.4676	9495		
Difference	1.8002	1271	(= 1271/1.8002)	(= 8224 − (706 x 3.6674))

Different amounts of feed were allowed during periods 1 and 2, the corresponding heat productions were measured and the difference in heat production (9495 − 8224 = 1271 Cal) was divided by the difference in feed consumption (5.4676 − 3.6674 = 1.8002 kg) to obtain the average heat increment per unit feed increment (1271/1.8002 = 706 Cal/kg). The net energy was then computed by deducting the heat increment from the metabolizable energy. The fasting heat production was computed by deducting the product of the heat increment per kg feed and the number of kg feed consumed, from the heat production at a given plane of consumption [8224 − (706 x 3.6674) = 5635].

[17] Armsby, H. P., "The Nutrition of Farm Animals", 1917.

While discussing the general principles relating net to gross energy intake, we learned many important details. Thus (Fig. 5.3) the apparent heat increment, or *SDA*, of feeding, as conventionally defined, ranges in cattle from 3 per cent of the *gross energy* at 0.5 maintenance to about 20 per cent at full feed; or it ranges from 8 per cent of the *TDN energy* at 0.5 maintenance to 30 per cent of the *TDN* energy at full feed; or it ranges from about 8 per cent of the *metabolizable energy* at 0.5 maintenance to 38 per cent of the metabolizable energy at full feed. The apparent range is less striking for the other excreta. The various energy categories of feed declined correspondingly with increasing plane of nutrition. Thus the digestible energy declines from 3.3 Cal/g feed at 0.5 maintenance to 3.0 Cal/g gross feed at full feed; the metabolizable energy declined from about 3.0 Cal/g feed at 0.5 maintenance to about 2.5 Cal/g feed at full maintenance; the net energy declined from about 2.3 Cal/g feed at 0.5 maintenance to 1.6 Cal/g feed at full maintenance. For purposes of computing efficiency, it is assumed in this book that 1 g *TDN* is equivalent to 4 Cal, or 1 pound *TDN* to 1814 Cal, corresponding to the 4 Cal/g of metabolizable energy, or physiologic fuel value, employed in computing human food values. The actual metabolizable energy per unit *TDN* of the usual cattle feeds appears to be less than those here given, of the order of 1600 Cal per pound *TDN*.

An interesting aspect of this analysis is that while the *apparent* digestibility of the rabbit ration (65 per cent of the gross energy) is about 8 per cent below that of the cattle ration (73 per cent of the gross energy), the apparent metabolizable and net-energy values are the same for both species (the metabolizable energy is about 60 per cent of the gross energy and the net is about 50 per cent of the gross energy). This apparent 8 per cent difference in digestibility is attributed to an 8 per cent greater methane production in cattle than in rabbits, and because the methane energy is conventionally counted as part of the digestible but not of the metabolizable energy. It thus appears that the rabbit is a good assay animal for estimating the metabolizable- and net-energy values of cattle rations, but that the *apparent* digestibility of the ration is, perhaps, 8 per cent less in rabbits than in cattle. The *real* digestibility is probably the same in both.

A curious aspect about the methane and urinary energy is that the percentages of both appeared to decrease with increasing plane of nutrition. The urinary energy appeared to be about 5 per cent of the gross feed energy at 0.5 maintenance and 2 3 per cent at full feeding. The methane energy declined from about 10 per cent at 0.5 maintenance to about 8 per cent at full feed.

The principle of diminishing returns was also applied to normal growth (successive time units elicit ever smaller weight gains), to egg production, to muscular work, and especially to milk production. The gross energetic efficiency of these processes increases with increasing rate of productivity because of declining maintenance cost per unit product; but the increasing gross efficiency occurs at declining increments because the gross efficiency approaches net efficiency (not including maintenance) as a limit.

The increase in milk production at decreasing increments with increasing grain consumption was explained by a different mechanism. Whatever the mechanism, the fact is that by increasing the grain allowance to the limit, milk production may be increased 15 to 20 per cent above the level of cows fed in accordance with the usual standards; and that milk production may be decreased by about 20 per cent on reducing the customary feeding standards by 20 to 30 per cent. The relative profitableness of heavy and light grain feeding depends, of course, on (1) the relative feed and milk prices and (2) the relative abilities of individual cows to utilize the extra grain allowance advantageously. The lactation problem will be discussed in greater detail in Chapters 21 and 22. The relative gross energetic efficiencies of various transformations (growth, milk production, egg production, muscular work) in different species and at different ages are discussed in Chapter 3.

Chapter 6

Metabolic Catalysts in the Efficiency Complex: Enzymes, Minerals, and Vitamins in Biologic Oxidations

> Among the most fundamental of the dynamic chemical events related to life are the oxidations which yield energy to the cell. *F. G. Hopkins*

> Oxidation was thought a few decades ago to be exceedingly simple. The organic molecule was burned and energy produced much as in the steam engine. There was no problem at all. Since then the problem of oxidation has developed into a wide and fruitful field of scientific inquiry. *Albert von Szent-Györgyi*

> There is a substance which even in very small quantities is of paramount importance to nutrition. If this substance is absent the appetite is lost and with apparent abundance the animals die of want. *C. A. Pekelharing,* 1905.

6.1: Introduction. The primary purpose of this book is to present quantitative analyses of metabolic processes of the organism *as a whole* in relation to the energetic efficiency of agriculturally productive transformations. This discussion would, however, fail in perspective if it overlooked the mechanisms of these processes. It is not the purpose to discuss the problems of biologic oxidation and catalysis in detail, but to outline in general fashion the contemporary theories and to point out the unity in what appears to be a confusing diversity of enzymes, vitamins, minerals, and hormones in biologic oxidation processes.

One aspect of biologic oxidation is that outside the body foodstuffs may be preserved for centuries, as illustrated by the good state of preservation of cereals recently found in the tombs of Egyptian kings, while within the body the nutrients are oxidized stepwise in accordance with needs of the organism. What are the mechanisms wherewith the body times the oxidation of the nutrients at the given rates in accordance with the needs of the organism?

Needless to say, the efficiency of biologic transformations is dependent on the exquisite timing and completeness of the oxidative reactions. Thus, to cite typical illustrations, the lack of thiamine (vitamin B_1) in the diet of species requiring it retards the oxidation rate of pyruvic acid and, therefore, leads to its accumulation in the tissues, which results in the well-known beriberi syndrome. Decrease of oxygen supply to the heart leads to angina pectoris, and lack of oxygen supply to the kidney (due to narrowing of blood vessels) leads o high blood pressure[1]. Intake of certain selenium compounds in the feed f farm animals leads to "alkali disease" in cattle due to the destruction of ertain oxidation catalysts[2]. Lack of the necessary traces of copper, zinc, nagnesium, iron, cobalt in animal feeds causes deficiency of oxidation catalysts in the body with serious symptoms variously named, depending on locality and species, such as salt sickness, marasmus, perosis, and so on. Whenever the oxidation process stops short of the final oxidation products H_2O and O_2, as for example when fat oxidation stops with the aceto-acetic acid stage, or arbohydrate oxidation with the pyruvic acid, lactic acid or alcohol stage, the energetic efficiency of food utilization is reduced by this much, in addition to development of the intoxications with corresponding pathologic conditions. Many disabilities associated with aging may be viewed as due in part to declining ability of the circulatory system to supply the tissues with oxygen and of the declining ability of the tissues to utilize the oxygen at a sufficiently rapid rate.

It is generally known[3] that food utilization is greatly depressed when the diet is deficient in vitamins. The depression of food utilization may be only apparent, due to anorexia[4] (diminished appetite), or real, as when the animals are pair-fed, and consume the same amounts of foods in the absence of anorexia. Thus Sure[5] reported (Fig. 6.1) that young rats, not suffering from anorexia, fed a diet deficient in riboflavin (vitamin B_2) gained about 6 g in 125 days, whereas litter mates receiving the same kind and amount of food for the 125 days but supplemented with 20 μg riboflavin gained about 60 grams—a ten-fold gain! Analogous results were reported by Shaw and Phillips[6] and others.

This difference in food utilization results in part from differences in completeness of food oxidation, as riboflavin is an essential component of about a dozen flavoprotein oxidation enzymes. It is known that decrease in dietary riboflavin decreases the corresponding flavoprotein enzymes, such as riboflavin-adenine dinucleotid[7], *d*-amino acid oxidase, or xanthin oxidase[8].

The problem of the mechanism and timing of biologic oxidation, no doubt a very old one, is new in its experimental aspects, beginning with the discoveries of Pasteur[9], Buchner[10], Harden and Young[11], Fletcher and Hopkins[12], Warburg[13], Wieland[14], and Thunberg[15], and continuing with the contemporary investigations on enzymes, vitamins, hormones, and minerals in nutrition[16].

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[1] Goldblatt, H., *et al.*, "Experimental hypertension", *J. Exp. Med.*, **59**, 343 (1934); **67**, 809 (1938); *J. Am. Med. Assn.*, **119**, 1192 (1942). Blackman, S. S., *Bull. Johns Hopkins Hosp.*, **65**, 353 (1939). Bent, R. J., and Zucker, M. B., "Intermediate pressor amine formation in the ischemic kidney", *J. Exp. Med.*, **24**, 235 (1941). Houssay, B. A., and Braun-Menendez, E., *Brit. Med. J.*, **2**, 179 (1942).

[2] Bernheim, F., and Klein, J. R., *J. Biol. Chem.*, **139**, 824 (1941).

[3] Johnson, S. R., Hogan, A. G., and Ashworth, U. S., Univ. Missouri Agr. Exp. Sta. Res. Bull. 246, 1936. Hogan, A. C., and Pilcher, R. W., *Id.*, Res. Bull. 195, 1933.

[4] Voris, A. L., Black, A., Swift, R. W., and French, C. E., *J. Nut.*, **23**, 555 (1942).

[5] Sure, B., *Id.*, **22**, 295 (1941).

[6] Shaw, J. H., and Phillips, P. H., *Id.*, **22**, 345 (1941).

[7] Ochoa, S., and Rossiter, R. A., *Biochem. J.*, **33**, 2008 (1939).

[8] Axelrod, A. E., Sober, H. A., and Elvehjem, C. A., *J. Biol. Chem.*, **134**, 749 (1940); **140**, 725 (1941).

The following sections outline some of this work rather superficially. Still there will be considerable overlapping of discussions due to the interrelations of the various subjects. The nutritional applications will be discussed in Chapter 20.

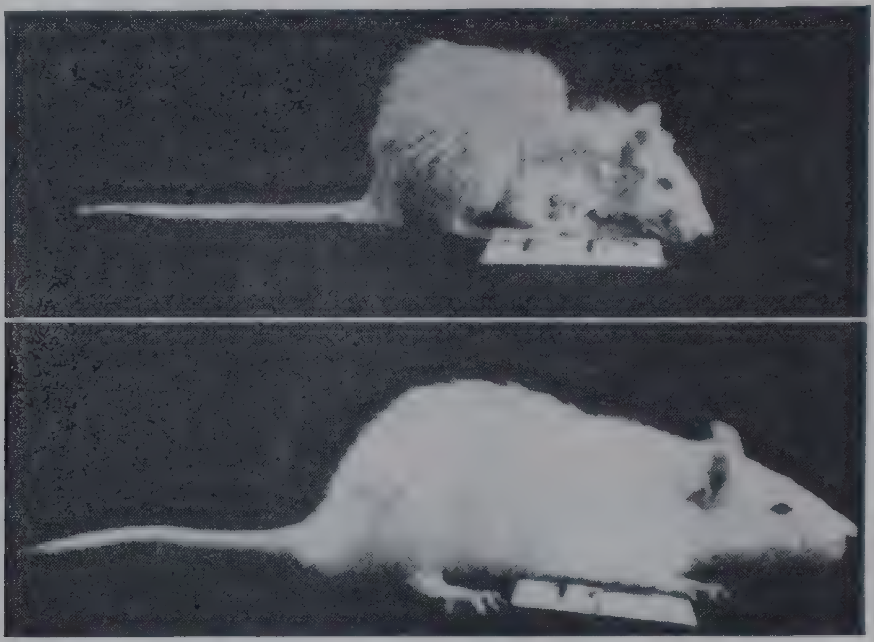

Fig. 6.1—The rats of the same initial weight and age consumed during 125 days equal amounts of food, but one of the pair received riboflavin (vitamin B_2) while the other did not. Acceptance of this result must await confirmation by a balance experiment with rigorous accounting for all income and outgo. Print by Barnett Sure, *J. Nutrition*, **22**, 299, 1941.

6.2: Aerobic and anaerobic oxidations with special reference to intense muscular work. Biologic oxidations are classed as (a) *respiratory*, occurring in the presence of oxygen and yielding H_2O and CO_2 as end products, and

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[9] Pasteur, L., *Ann. Chim. Phys.*, **58**, 323 (1860).

[10] Buchner, H., *Ber. deut. chem. Ges.*, **30**, 117 (1897).

[11] Harden, A., and Young, W. J., *J. Chem. Soc.*, **21**, 189 (1905); *Proc. Roy. Soc.*, **77B**, 405, 1906; Harden, A., "Alcoholic Fermentations", Longmans, 1932.

[12] Fletcher, W. M., and Hopkins, F. G., *J. Physiol.*, **35**, 247 (1907); and *Proc. Roy. Soc.*, **89B**, 444 (1917). Hopkins, F. G., *Biochem. J.*, **15**, 286 (1921); *J. Biol. Chem.*, **84**, 269 (1929).

[13] Warburg, O., *Biochem. Z.*, **113**, 257 (1921); **303**, 40 (1939); *Ergeb. Enzymforsch.*, **7**, 210 (1938).

[14] Wieland, H., *Ber. deut. chem. Ges.*, **47**, 2085 (1914) and *Ergeb. Physiol.*, **20**, 477 (1922).

[15] Thunberg, T., *Skand. Arch. Physiol.*, **35**, 163 (1918); **40**, 1 (1920); **43**, 275 (1923).

[16] For contemporary reviews, see *Ann. Rev. Biochem.* and *Ann. Rev. Physiology*; *Adv. Enzymology*; *Enzymologia*; *Ergeb. d. Enzymforschung*; *Cold Spring Harbor Symposia on Quantative Biology*, especially vol. **7**, 1939; *Biological Symposia*, Jaques Cattell Press, vols. **3** and **5**, 1941; "Symposia on Respiratory Enzymes", University of Wisconsin Press, 1942, "Symposium on Biological Action of Vitamins", Ed. by E. A. Evans, University of Chicago Press, 1941. Kalckar, H. M., "Energetic coupling in biological synthesis", *Chem. Rev.*, **28**, 71 (1941); *Biol. Rev.*, **17**, 28 (1942). Nord, F. F., "The mechanism of alcoholic fermentation", *Chem. Rev.*, **26**, 423 (1940). There are many important books, such as Stephenson, M., "Bacterial Metabolism", 1939, "Perspectives in Biochemistry", ed. by Joseph Needham and David E. Green, 1939; Oppenheim, C., and Stern, K. G., "Biological Oxidation", 1939. Bernheim, F., "Interactions of Drugs and Cell Catalysts", Burgess, 1942.

(b) *fermentative*, in which atmospheric oxygen does not participate, yielding incompletely oxidized products, such as pyruvic acid, lactic acid, acetic acid, alcohol, and so on. Corresponding to the respiratory and fermentative types of oxidation there are two types of organisms: (a) *aerobic*, depending for their energy on oxidation by atmospheric oxygen, and (b) *anaerobic*, depending for their energy on anaerobic oxidations. But there is no sharp dividing line between the two.

Thus, Pasteur[17] discovered that a plentiful oxygen supply causes yeast to transfer from the anaerobic to the aerobic method of oxidation ("Pasteur effect"[18]); and Fletcher and Hopkins[19] discovered that muscle of aerobic animals may be stimulated to work in the absence of oxygen, yielding lactic acid (a product of anaerobic oxidation) rather than CO_2 and H_2O.

Fletcher and Hopkins exercised an isolated muscle. But the same appears to be true in intact animals. Thus it will be shown in Chapter 24 that during *prolonged* hard work, horses and men may expend about eight-fold the energy at rest, whereas during *very intense* muscular work (which cannot be prolonged because of rapidly onsetting fatigue), they may expend 100 times the energy at rest. This does not mean that the rate of oxygen consumption is increased 100 times. During very intense exertion, when the oxygen supply is too slow for aerobic oxidation, the energy is obtained anaerobically, from anaerobic energy reservoirs. Under such conditions the animal is said to go into *oxygen debt*. Lactic acid accumulation is associated with anaerobic oxidation in animals. Hill[20] reported an athlete who liberated over 4 g of lactic acid per *second* while running at the rate of 11 yards per second. During the 15 seconds of sprinting, about 50 g ($1\frac{3}{4}$ oz) of lactic acid was liberated, and the *oxygen debt* reached 7 to 8 liters. But the oxygen debt is known to have risen in a 70-kg athlete to 19 liters, with the liberation of 114 grams ($\frac{1}{4}$ lb of lactic acid[21]).

Regardless of theories, the *fact* is that the "oxygen debt" is associated with *increase* in concentrations of lactic acid and phosphoric acid (and perhaps pyruvic acid) and also with a *decrease* in concentration of phosphocreatine and adenosine pyrophosphate. The "recovery" (at rest) phase is associated with a reverse process, *decrease* in concentration of lactic and phosphoric acids and *increase* in concentration of phosphocreatine and adenosine pyrophosphate[22, 23]. It thus appears that when aerobic oxidation is inadequate, the energy is obtained by cleavage of phosphocreatine (also called phosphagen and creatine phosphate) to creatine and phosphate.

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[17] Pasteur, L.[9], "Studies in Fermentation", 1876.

[18] Dixon, K. C., "The Pasteur effect", *Biol. Rev.*, **12,** 431 (1937). Burk, D., "The Pasteur effect", *Cold Spring Harbor Symposia on Quantitative Biology*, **7,** 420 (1939). Stern, K. G., Melnick, J. L., and DuBois, D., "The Pasteur enzyme", *Science*, **91,** 436 (1940).

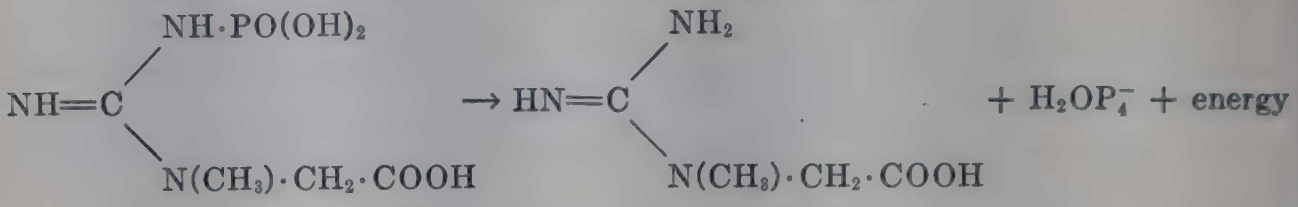
[19] Fletcher, W. M., and Hopkins, F. G., *J. Physiol.*, **35,** 247 (1907).

[20] Furusawa, K., Hill, A. V., and Parkinson, J. L., "The dynamics of 'sprint' running", *Proc. Roy. Soc.*, **102B,** 50 (1927).

[21] Hill, "Muscular movements in man", New York, pp. 30–32, 1927.

[22] Lundsgaard, E., *Biochem. Z.*, **217,** 162; **227,** 51 (1930); *Harvey Lectures*, **33,** 65 (1938).

[23] See Eggleton, P., and Eggleton, G. P., "A labile form of organic phosphate", *Biochem. J.*, **21,** 190 (1927). The phosphocreatine was isolated from muscle filtrate by Fiske,



$$NH{=}C\begin{cases}NH\cdot PO(OH)_2\\ N(CH_3)\cdot CH_2\cdot COOH\end{cases} \rightarrow HN{=}C\begin{cases}NH_2\\ N(CH_3)\cdot CH_2\cdot COOH\end{cases} + H_2OP_4^- + \text{energy}$$

(*phosphocreatine*) (*creatine*)

During recovery, phosphocreatine is resynthesized at the expense of another energy source. The recurrent synthesis and cleavage of phosphocreatine and adenopyrophosphate is thus analogous to recurrent charging and discharging of a battery. Phosphocreatine, like a battery, is an energy reservoir, discharged and charged in accordance with the conditions and needs. Lohman discovered that adenyl pyrophosphate is the phosphate carrier; it furnishes the phosphate for phosphorylation of the creatine, as indicated by the Lohman reaction:

$$\text{adenyl pyrophosphate} + \text{creatine} \rightarrow \text{creatine phosphate} + \text{adenylic acid}$$

The energy for resynthesis (charging) of the phosphocreatine may come from the oxidation of glycogen to CO_2 and H_2O

$$H_3PO_4 + \text{creatine} + \text{glycogen} + O_2 \rightarrow \text{phosphocreatine} + CO_2 + H_2O$$

and perhaps from fermentation (glycolysis) of glycogen to lactic acid.[24]

Lactic acid formation is not believed to be the *direct* energy source for anaerobic muscular contraction, since the lactic acid forms *after* the work of contraction[25], as indicated by the observation that muscular contraction may occur and carbohydrate may be oxidized after poisoning the muscle with iodoacetate when lactic acid formation is blocked[26, 27], and that up to a certain level the oxygen debt is incurred without increase in blood lactate[26, 28]. According to Dill[28], the recovery period is, therefore, made up of (1) an alactacid and (2) a lactacid phase.

6.3: Oxidation-reduction potentials and biologic oxidation. It was said above that oxidations are of two kinds: (1) aerobic, involving atmospheric oxygen, and (2) anaerobic, in which oxygen does not participate. In other words, while oxidation may mean combination with oxygen, it is not necessarily such. More often oxidation means the loss of hydrogen, or dehydro-

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C. H., and Subbarow, Y., *Science*, **65**, 401 (1927); **67**, 169 (1928); *J. Biol. Chem.*, **81**, 629 (1929).

[24] Meyerhof, O., *Ergeb. Physiol.*, **39**, 10 (1937); *Biochem. Z.*, **65** (1938); Lundsgaard, E., *Id.*, **217**, 227 (1930); *Ann. Rev. Biochem.*, **7**, 377 (1938).

[25] Embden, G. T., *Z. Physiol. Chem.*, **151**, 209 (1926).

[26] Lundsgaard, E.[22]; Barker, S. B., and Shorr, E., *J. Biol. Chem.*, **129**, 33 (1939).

[27] Johnson, R. E., and Edwards, H. T., *J. Biol. Chem.*, **118**, 427 (1937). Sacks, J., *et al.*, *Am. J. Physiol.*, **118**, 69, 232 (1937); **122**, 215 (1938). Hill, D. K., *J. Physiol.*, **98**, 207 (1940). Millikan, G. H., *Proc. Roy. Soc.*, **123B**, 218 (1937).

[28] Margaria, R. E., Edwards, H. T., and Dill, D. B., *Am. J. Physiol.*, **106**, 689 (1933).

nation. But oxidation is not confined to gain of oxygen and/or loss of ydrogen; and reduction is not confined to loss of oxygen or gain of hydrogen. roadly defined, oxidation is loss of electrons, and reduction is gain of electrons. Thus ferrous iron, Fe^{++}, is oxidized by the loss of an electron, *e*:

$$Fe^{++} - e \rightarrow Fe^{+++}$$

r ferric iron, Fe^{+++}, is reduced by the gain of an electron, *e*:

$$Fe^{+++} + e \rightarrow Fe^{++}$$

his oxidation, or reduction, may involve oxygen

$$2FeO + O \rightarrow Fe_2O_3$$

r may not involve oxygen

$$FeCl_2 + Cl \rightarrow FeCl_3$$

The experimental work on biologic-oxidation mechanisms is concerned nostly with anaerobic processes often conducted near freezing temperatures ecause the aerobic processes at 37°C are too rapid for detailed observation nd analysis, or by "dissecting out" metabolic stages by differentially acting metabolic inhibitors or poisons, such as iodoacetates, fluorides, cyanides, and so on. Because of the difficulty of observing the details of normal aerobic processes, it is not definitely established that most of the products formed in tissues under anaerobic conditions, such as pyruvic acid, lactic acid, alcohol[29] and so on, are necessarily formed under aerobic conditions of rest. It is certain, however, as indicated in the preceding section, that when the circulatory oxygen supply is inadequate, energy expenditure is associated with increased concentration of lactic acid, a typical product of anaerobic oxidation; and that the absence of dietary thiamine involved in pyruvic acid oxidation leads to the accumulation of pyruvic acid[30], a typical product of anaerobic oxidation. Moreover, tissues or systems normally poorly supplied with oxygen tend to have appreciable concentrations of lactic acid. Spermatozoa[31] regularly obtain energy by glycolysis (fermentation of glucose to lactic acid), and there is no doubt that there is more or less glycolysis in other animal systems.

While the definition of oxidation as loss of electrons and reduction as gain of electrons is an old one in general chemistry, its elucidation and general acceptance in biology is recent. It is due largely to Mansfield Clark[32], who defined dehydrogenase activity as the taking up and passing of electrons.

When a solution of Fe^{++} is connected with one of Fe^{+++}, an electromotive force is created, the magnitude of which depends on the relative concentrations of the two ion forms. Potential differences are likewise set up if solutions of any two electrolytes are connected. The voltage reading will depend on the relative "electron pressures" of the respective elements. This way, the elements were arranged in an electromotive series, in some such order as the following: Li, Rb, K, Sr, Ba, Ca, Mg, Al, Mn, Zn, Cr, Fe, Cd, Co, Ni, Sn, Pb, H, Sb, Bi, As, Cu, Hg, Ag, Pt, Au, which is the order of ease with which the elements donate their electrons, that is, become oxidized. The electromotive potentials of the inorganic elements are known. The potential driving the reduction of H^+ by Zn^0 in the reaction,

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[29] There is normally from 0.05 to 0.12 mg alcohol per 100 g brain, from 0.09 to 0.23 mg alcohol per 100 g liver, from 0.04 to 0.14 mg alcohol per 100 g kidney, and so on [Harger, R. N., and Gross, A. L., *Am. J. Physiol.*, **112**, 374 (1935)].

[30] Peters, R. A., *Biochem. J.*, **31**, 2240 (1937).

[31] Moore, B. H., and Mayer, D. T., "Metabolism of semen", Univ. Missouri Agr. Exp. Sta. Res. Bull. 338, 1941.

[32] Clark, W. M., Hygienic Laboratory, U. S. Public Health Service, Bull. 151, 1928.

$$Zn^0 + 2H^+ \rightarrow Zn^{++} + H_2^0$$

for example, is definitely known from electrode potential measurements.

Moreover, the free energies of the reactions are known [Sect. 2.1.2 and eq. (2.5)]; the free energy, ΔF, of a reversible galvanic cell is related to its potential, E, by the equation

$$\Delta F = -nFE \tag{2.5}$$

and the potential, E_h, with respect to the hydrogen electrode taken as zero, is computed from the equation

$$E_h = E_0 + \frac{RT}{nF} \ln \frac{\text{concentration oxidized form}}{\text{concentration reduced form}}$$

This equation was previously cited [eq. (2.8), sect. 2.1.2]. E_o is the characteristic constant of the system when the half cell of the given substance is connected to a hydrogen electrode, that is, to platinum sponge saturated with hydrogen gas, when the concentration of the oxidized form is equivalent to the concentration of the reduced form and when the pH is 7.0 at 30° C; R is the gas constant, 8.31507 volt coulombs; n, number of equivalents, or electrons, freed when the reduced form is changed to the oxidized form; F is the Faraday (96,500 coulombs); ln represents the natural logarithm.

Living cells contain many substances which, like the above inorganic elements, may be arranged in an electromotive series. The electromotive-series arrangement of substances in the body cannot be as precise as that of inorganic elements acting in glass beakers because of the enormously greater complexity of the thermodynamic equilibria in the body. But such EMF arrangements are useful for prediction purposes.

There is a large literature[33] on the oxidation-reduction potentials of various biological substances—enzymes and substrates—involved in biologic oxidations. Many artificial dyes, such as methylene blue, made famous by Thunberg, who used it as an oxidizing agent in biologic systems (in place of oxygen), change color at certain oxidation-reduction zones and are thus used as indicators for measuring O-R potentials. When thus arranged in an electromotive series, oxygen is on top, with the highest positive voltage, and hydrogen at the bottom, with the highest negative voltage. The various biologically active substances come in between.

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[33] For review, see: Ball, E. G., in "Symposium on Respiratory Enzymes", University of Wisconsin Press, 1942; Barron, E. S. G., *Physiol. Rev.*, **19**, 184 (1939); Stephenson, M.[16]; Kalckar, H. M., 1941[16]; Gillespie, L. J., *Soil Sci.*, **9**, 199 (1920); Clark, W. M., *Pub. Health Rep.*, **38**, 443 (1923); *Medicine*, **13**, 207 (1934); *J. App. Physics*, **9**, 97 (1928); Clark, W. M., "Determination of Hydrogen Ions", 1928; Michaelis, L., "Oxidation-reduction Potentials", 1930. Hewitt, L. F., "Oxidation-reduction potentials in bacteriology and biochemistry", London, 1935; Shaffer, P. A., *J. Phys. Chem.*, **40** (1936); Wurmser, R., "Oxydations et reductions", Paris, 1930.

Nutrients are, of course, reducing agents; by this we mean that they tend to be oxidized, to lose their hydrogens, and these, therefore, come low in the electromotive series, near hydrogen, which is assigned a voltage of about −0.4 for pH 7.0. The hydrogens (and electrons) from the substrate are transported, *stepwise*, from one carrier or mediator, or from one H transport system or H-acceptor to the other standing above it in the EMF series, until finally the substrate hydrogen reaches the atmospheric oxygen standing at the top of the series, forming water, the final step in the oxidation process in aerobes. The essential oxidation feature is the combination of hydrogen with oxygen (or the transfer of electrons from hydrogen to oxygen), not the combination of carbon with oxygen.

As previously noted, the position of the substrate fuel in the EMF series is low, near hydrogen, with a voltage reading of about −0.4. Then come[34] the pyridinoprotein enzymes (voltage about −0.3), followed by the flavoprotein enzymes (voltage about −0.1 to −0.2), followed by the iron-porphyrin enzymes, namely cytochrome-*b*(−0.04), cytochrome-*c*(+0.27), and cytochrome-*a*(+0.29); followed by the cytochrome oxidases (+0.4 to +0.6) and, finally, oxygen (+0.8).

The stepwise reductions, that is the successive passing of the hydrogens or electrons, is thus from the substrate to the pyridine nucleotides, to the flavoproteins, to the cytochromes and cytochrome oxidases, and finally to oxygen. In other words, the substrates reduce the pyridinoprotein enzymes, which reduce the flavoprotein enzymes, which reduce the porphyrin enzymes, which reduce the atmospheric oxygen. This is an oversimplified diagram, but it may give a general idea of the way biologic, stepwise oxidations occur.[35]

The first step in oxidation is the phosphorylation (combination with phosphoric acid) of the glycogen or glucose, forming hexose phosphate; this splits into triose phosphates; then into glyceraldehyde, as indicated in the following over-simplified diagrams for oxidation of hexose and for oxidative deamination of amino acid.

$$\text{I.}\quad C_6H_{12}O_6 \xrightarrow{\text{phosphorylase}} \underset{\textit{hexose diphosphate}}{C_6H_{10}O_4\cdot 2H_2PO_4} \longrightarrow \underset{\textit{triose phosphate}}{2C_3H_5O_2\cdot H_2PO_4} \xrightarrow{\text{dehydrogenase}}$$

$$\underset{\textit{glycerylphosphate}}{CH_2OH\cdot CHOH\cdot CH_2\cdot H_2PO_4}$$

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[34] *Cf.* Ball, E. G.[33]

[35] For another aspect, see Szent-Györgyi, A., "Towards a new biochemistry", *Science*, **93**, 609 (1941).

$$\text{and } \underset{\textit{glyceric acid phosphate}}{H_2PO_4 \cdot CH_2 \cdot CHOH \cdot COOH} \longrightarrow \underset{\textit{lactic acid}}{CH_3 \cdot CHOH \cdot COOH}$$

$$\text{and } \underset{\textit{pyruvic acid}}{CH_3 \cdot CO \cdot COOH} \xrightarrow{\text{carboxylase}} CO_2 + CH_3CHO \ (?)$$

$$\text{II. } \underset{\textit{α-amino propionic acid}}{CH_3 \cdot CHNH_2 \cdot COOH} \xrightarrow{\text{dehydrogenase}} \underset{\textit{α-imino propionic acid}}{CH_3 \cdot C{=}NH \cdot COOH} \longrightarrow$$

$$\underset{\textit{pyruvic acid}}{CH_3 \cdot CO \cdot COOH} + \underset{\textit{urea}}{(NH_2)CO}$$

These and similar oxidoreduction reactions are catalyzed by enzyme systems, of which the following are outstanding. (1) Phosphorylases, catalyze phosphorylation, that is, combination of phosphate with glycogen, starch, glucose, and so on, preliminary to cleavage.[36] (2) Decarboxylases, exemplified by carboxylase, which splits CO_2 from α-keto acids converting them to aldehydes and CO_2, and by carbonic anhydrase which splits H_2CO_3 into CO_2 and H_2O. (3) Dehydrogenases typified by lactic acid dehydrogenase, which converts lactic acid to pyruvic acid; amino acid oxidase[37] or dehydrogenase, which converts α-amino to α-keto acids; succinic acid dehydrogenase, which converts succinic acid to fumaric acid; cytochrome reductase, which converts reduced coenzyme II to oxidized coenzyme II; and alcohol dehydrogenase, which converts alcohol to acetaldehyde. (4) Oxidases, including cytochrome oxidase (also called Warburg's enzyme or *Atmungsferment*, Ehrlich's enzyme, and indophenol oxidase), which catalyzes the oxidation (by oxygen) of reduced cytochrome-c to (oxidized) cytochrome-c (equations given below); tyrosinase, which oxidizes tyrosine to black pigments (seen in darkening of cut potato or apple); and polyphenol, which convert polyphenols to quinones. (5) Transaminases[38], or aminophorases, which catalyze intermolecular transfer of the amino group and a hydrogen group as, for example, the transfer of paired amino and keto acids to corresponding keto and amino acids. The place of vitamins and minerals in these biocatalytic systems—enzymes and coenzymes—is discussed below and also in Chapter 20.

The following examples indicate empirical applications of oxidation-reduction (O-R) potentials in the dairy industry. The O-R of milk normally drifts down with time after milking, probably due to the oxygen removal by aerobic bacteria or by other oxidations. If, however, copper or iron is added (the potency of copper is ten times that of ferrous[39] iron), the O-R potential rises, and oxidized flavors develop in parallel[40]. On the other hand, tin and aluminum lower the O-R potential of milk, and probably retard the flavor production[41]. Changing dairy cows from dry to fresh feed decreases the O-R[42] and reduces development of oxidized flavors. Summer milk does not develop oxidized flavors as readily as winter milk, and the O-R potential of summer milk is below that of winter milk[43]. This may be associated with the increased ascorbic acid content in summer milk: increasing ascorbic acid (reduced form) decreases the O-R potential, as can be proved by adding crystalline ascorbic acid to milk[39]. In brief, anything which reduces the O-R potential of milk also reduces the production of oxidized flavors in milk[44].

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[36] See the long series of reports by Cori[51] *et al.*, beginning with *J. Biol. Chem.*, **121,** 465 (1937), the latest being *J. Biol. Chem.*, **151,** 21 (1943).

[37] Krebs, H. A., *Biochem. J.*, **29,** 1620 (1935).

[38] Cohen, P. P., "Transamination", *Federation Proc.*, **1,** 273 (1942).

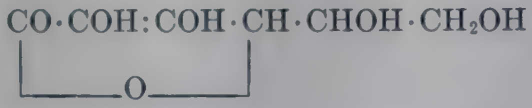
[39] Swanson, A. M., and Sommer, H. H., *J. Dairy Sci.*, **23,** 597 (1940). Dahle, C. D., and Palmer, L. S., Pennsylvania Agr. Exp. Sta. Bull. 347 (1937).

[40] Tracy, P. H., Ramsey, R. J., and Ruehe, H. A., Ill. Agr. Exp. Sta. Bulls. 389, 1933, and 407, 1934.

Off flavor in plant products, such as a hay-like flavor in stored raspberries, is probably also the result of oxidations similar to those in milk, butter, and ice cream. The removal of oxygen, or what is more practical the maintenance of an atmosphere of high N_2 or CO_2 concentration, is often a means of preserving food products by reducing oxidation processes initiated by the various catalysts in the tissues.

6.4: Interrelations between minerals, vitamins, enzymes, and hormones in biologic oxidations: an illustration of unity in diversity. Keilin[45] recognized the identity in what were considered as several distinct enzymes, namely Warburg's enzyme (*Atmungsferment*), indophenyl oxidase (Ehrlich's enzyme, 1885), and cytochrome oxidase.

Szent-Györgyi[46], and also King[47], recognized that the coenzyme *l*-ascorbic acid,



$$\underbrace{\mathrm{CO\cdot COH{:}COH\cdot CH}}_{\mathrm{O}}\mathrm{\cdot CHOH\cdot CH_2OH}$$

is identical with the antiscorbutic factor, vitamin C. This discovery of the relation between a vitamin and enzyme in biologic oxidation is important partly because it focuses attention on the convergence of several apparently different kinds of investigations into one, namely biocatalysis. Szent-Györgyi was awarded the 1937 Nobel Prize in medicine for this and related discoveries.

6.4.1: Definitions and interrelations. Vitamins are organic catalysts, or essential components of catalysts, in biologic oxidations and related processes.

Vitamins are *exogenous catalysts*, externally provided; hormones and enzymes are *endogenous catalysts*, internally produced by the body.

There is, however, no dividing line between the exogenous and endogenous catalysts. Thus ascorbic acid (vitamin C) is an *exogenous catalyst* to primates and guinea pigs: they must ingest ascorbic acid; they cannot synthesize it. Other animal species examined are not dependent on dietary ascorbic acid—to them ascorbic acid is an *endogenous catalyst*; they can synthesize it. Of course, green plants synthesize ascorbic acid, so that it is not a vitamin to plants.

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[41] Thurston, L. M., "Proc. Intern. Assn. Milk Dealers, Lab. Sect.", p. 121, 1935.

[42] Greenbank, G. R., *J. Dairy Sci.*, **21,** 144 (1938).

[43] Webb, R. E., and Hileman, J. L., *Id.*, **19,** 476 (1936).

[44] Greenbank, G. R., *Id.*, **23,** 725 (1940).

[45] Keilin, D., and Hartree, E. F., *Proc. Roy. Soc.*, **104B,** 206 (1929); **119B,** 114 (1936); **121B,** 173 (1936); **122B,** 298 (1937).

[46] Szent-Györgyi, A., *Biochem. J.*, **22,** 1387 (1928); *J. Biol. Chem.*, **90,** 385 (1931). Haworth, W. N., and Szent-Györgyi, *Nature*, **131,** 24 (1933). Tauber, H., Kleiner, I. S., and Mishkind, D., *Proc. Soc. Exp. Biol. Med.*, **32,** 577 (1935); *J. Biol. Chem.*, **110,** 211 (1935). Szent-Györgyi, A., *Biochem. J.*, **26,** 865 (1932); **27,** 279 (1933).

[47] King, C. G., *et al.*, *J. Biol. Chem.*, **94,** 483, 491 (1931-2); **97,** 325 (1932). King, *Physiol. Rev.*, **16,** 238 (1936); *J. Am. Med. Assn.*, **111,** 1098, 1555 (1938).

Moreover, even the self-sufficient animals are not always self-sufficient. Low vitality, due, for example, to low vitamin A intake[48], or to increasing age[49], results in low ascorbic-acid production, in which case ascorbic-acid administration is indicated.

Hormones and enzymes are endogenous catalysts; however, the building stones of these endogenous catalysts are derived from food, an exogenous source. Thus thyroxine, the powerful thyroid biologic-oxidation catalyst, is produced from food components, from the mineral iodine and from the amino acid tyrosine, which the body must obtain from food. Similar statements may be made of other hormones, such as adrenaline, another tyrosine derivative (Ch. 7).

Broadly speaking, an oxidoreduction *enzyme* is a protein-complex catalyst of high molecular weight, not dialyzable, and denatured by heat. The enzyme contains, or is associated with, a *coenzyme* which is of relatively small molecular weight, dialyzable, and may be thermostable. The "active part" of the enzyme or coenzyme is the *prosthetic group*.

Now some vitamins serve as prosthetic groups in enzyme systems. The best known example of such vitamins is vitamin B_1, or thiamine, which is the prosthetic group of the coenzyme cocarboxylase, a pyrophosphoric acid ester of thiamine. The cocarboxylase is, in turn, the prosthetic group of the enzyme carboxylase previously mentioned, which is a pyrophosphothiamine magnesium protein[151]. This enzyme carboxylase catalyzes the decarboxylation of α-keto acids, particularly pyruvic acid. If there is deficiency of thiamine, there is also deficiency of the coenzyme cocarboxylase and of the enzyme carboxylase with the associated high level of pyruvic acid[30] and polyneuritis syndrome (Sect. 20.6). The reaction equations under the influence of carboxylase (decarboxylation of pyruvic acid) and dehydrogenases (conversion of triose phosphate to phosphoglyceric acid, and oxidative deamination of amino acid) were cited in the preceding section.

Vitamin B_2, or riboflavin, is similarly the prosthetic group of the coenzyme riboflavin mononucleotide, which is in turn the prosthetic group of dehydrogenase enzymes, such as Warburg and Christian's "yellow enzyme" and of the dehydrogenase enzyme cytochrome reductase, previously described. There are many riboflavoprotein enzymes catalyzing oxidation processes. The coenzyme riboflavin adenine dinucleotide is a prosthetic group, among others, of the enzyme xanthine oxidase, and xanthine oxidase and riboflavin dinucleotide decrease during dietary riboflavin deficiency[7].

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[48] Sutton, T. S., *et al.*, *J. Biol. Chem.*, **144,** 183 (1942).

[49] Phillips, P. H., *et al.*, *J. Dairy Sci.*, **23,** 873 (1940); **24,** 153 (1941). *Holstein Friesian World*, **39,** 369 (1942).

Nicotinic acid is similarly the prosthetic group of the coenzymes I and II (also known as codehydrogenases I and II and by other designations), which are, respectively, diphosphopyridine and triphosphopyridine nucleotides (containing nicotinic acid or pyridine groups, adenine, phosphoric acid, and a pentose). The pyridine nucleotides are in turn prosthetic groups of the dehydrogenase enzymes which catalyze oxidation of lactate, malate, β-hydroxybutyrate, glyceraldehyde diphosphate, citrate, glutamic acid, glucose-6-phosphate, alcohol, succinate, formate, aldehydes and other substrates previously mentioned. Some inorganic elements, such as iron, function as prosthetic groups in enzyme systems similar to that of vitamins (Ch. 20).

Phosphorylation of the substrate (glucose, glycogen, and so on) is prerequisite for all biologic oxidations, aerobic and anaerobic[51]. The ubiquitous participation of phosphates in biologic oxidation is, in fact, one of its most impressive features. There is a long series of phosphate esters, such as hexosemonophosphate, hexosediphosphate, glycerophosphate, phosphoglyceric ester, phosphopyruvic ester, and so on, often associated with the names of their discoverers, such as the Harden-Young ester (fructose-1,6-diphosphate), Neuberg ester (fructose-6-phosphate), Robison ester (glucose-6-phosphate), Cori ester (glucose-1-phosphate) and so on, which play an important part in oxidoreductions.

6.4.2: Minerals in biologic oxidation. As explained above, phosphate occupies a key position in biologic oxidation. Pasteur observed its importance in 1860, Harden and Young confirmed it in 1905, and it is currently under intensive investigation by the Cori, Lipmann and Meyerhof schools, and by others.

As explained in connection with phosphocreatine (Sect 6.2) some phosphate esters serve as temporary biologic energy reservoirs, analogous to charged batteries. Thus, according to Cori, the synthesis of 6 molecules of glucose phosphate is coupled, or associated, with the oxidation of one molecule of glucose. A mol of glucose phosphate, therefore, has a labile energy increment which, depending on the energetic efficiency of the process, may be as high as 115 Cal ($\frac{1}{6}$ of about 700 Cal, the free energy of glucose). This is, presumably, what Lipmann[51] refers to as phosphate-ester bond energy, the main form or source of anaerobic energy as illustrated by the reactions:

$$\text{glycerophosphate} + H_2O \rightleftharpoons \text{glycerol} + \text{phosphate} + \text{energy}$$

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[51] Lipmann, F., *Advances in Enzymology*, **1,** 99 (1941). Cori, C. F., and Cori, G. T., *Ann. Rev. Biochem.*, **10,** 151 (1941). Sowden, J. C., and Fischer, H. O. L., *Ann. Rev. Biochem.*, **11,** 203 (1942). Meyerhof, O., *Cold Spring Harbor Symposia on Quantitative Biology*, **3,** 239 (1941). Cori, G. T., Colowick, S. P., and Cori, C. F., *J. Biol. Chem.*, **123,** 375 (1938). Colowick, S. P., Welch, M. S., and Cori, C. F., *Id.*, **33,** 359, 641 (1940). Kalckar, H. M., *Biol. Rev.*, **17,** 28 (1942), and *Enzymologia*, **6,** 143 (1939).

As the value of the equilibrium constant, K, is[52] about 40 at 38°C, we have the equation

$$\Delta F^\circ = -RT \log K = -4.58T \log K = -4.58 \times 311 \times \log 40 = -22.8 \text{ Cal}$$

The phosphate group also catalyzes the oxidation and transport of fats[53]. Other inorganic elements may participate in the oxidation of fat and perhaps in its transformation to carbohydrate[54].

Pasteur also observed that magnesium has an important function in yeast fermentation, and it appears from the work of Cori, Lohmann, Ochoa, and others that Mg^{++}, Mn^{++}, and perhaps Co^{++}, may activate cozymases, dehydrogenases, carboxylases, phosphatases, phosphoglycomutases, cholestorinases, and that Mg is involved in the phosphorylation of enzyme systems. Carboxylase is a diphosphothiamine-magnesium protein[55].

Probably because of its other activation effects, such as that on bone phosphatase[56], manganese deficiency, as observed on chickens, leads to leg-bone malformations, called perosis[57]. However, other deficiencies, such as of biotin and choline, also lead to perosis[58].

Manganese has other functions[59]. Its deficiency in young rats leads to testicular degeneration[60], subnormal vitality of the fetus and the new born[61], and abnormal maternal behavior including unsatisfactory lactation[62]. Manganese deficiency also leads to a profound depression of hatchability of eggs (5 per cent of normal when the manganese in the ration is reduced to 40 ppm) and the embryos show chondrodystrophy[63]. Manganese may play an important part in the synthesis of ascorbic acid[64].

Iron is another conspicuous inorganic element involved in biologic oxidation. It is the prosthetic group of the hemins. Hemoglobin, the red pigment in the blood, is the best known hemin complex. The body of the average adult man contains about 6 liters (or quarts) of blood; the blood contains about 160 grams hemoglobin per liter; the red blood cells contain about 32 per cent hemoglobin; hemoglobin contains about 0.33 per cent iron. The iron content of a 70-Kg human body is about 4 g.

[52] Kay, H. D., *Biochem. J.*, **22,** 855 (1928).

[53] Bloor, W. R., "Fat transport in the animal body", *Physiologic Reviews*, **19,** 557 (1939). Chaikoff, I. L., "Phospholipoid metabolism", *Id.*, **22,** 291 (1942).

[54] McHenry, E. W., *Science*, **86,** 200 (1937). McHenry and Gavin, G., *J. Biol. Chem.*, **134,** 683 (1940); **138,** 471 (1941).

[55] Green, D. E., *et al.*, *J. Biol. Chem.*, **135,** 795 (1940); **138,** 327 (1941).

[56] Wiese, A. C., Elvehjem, C. A., Hart, E. B., *et al.*, *Poultry Sci.*, **20,** 255 (1941).

[57] Wilgus, H. S., Norris, L. C., and Heuser, P. H., *J. Nut.*, **14,** 155 (1937). Caskey, G. D., Gallup, W. D., and Norris, L. C., *Id.*, **17,** 407 (1939). Wilgus, H. S., and Patton, A. R., *Id.*, **18,** 35 (1939).

[58] Richardson, L. R., Hogan, A. G., and Miller, O. N., "Relation of biotin to perosis", Univ. Missouri Agr. Exp. Sta. Res. Bull. 343, 1942. Hegsted, D. M., *et al.*, *J. Nut.*, **23,** 175 (1942). Jukes, T. H., and Almquist, H. J., *Ann. Rev. Biochem.*, **11,** 516 (1942).

[59] Gilman, H., "Organometallic compounds in biology", *Science*, **93,** 47 (1941).

[60] Orent, E. R., and McCollum, E. V., *J. Biol. Chem.*, **92,** 651 (1931).

[61] Daniels, A. L., and Everson, G. J., *J. Nut.*, **9,** 191 (1935).

[62] Skinner, J. T., and Steenbock, H., *Am. J. Physiol.*, **101,** 591 (1932).

[63] Lyons, M., and Insko, W. M., Kentucky Agr. Exp. Sta. Bull. 37, p. 61, 1937.

[64] Rudra, M. M., *Nature*, **144,** 668 (1939).

The divalent iron atom occupies a central position in the hemin part of hemoglobin, binding, centrally, four pyrrol rings together into a tetrapyrrol complex, while four CH bridges bind the four pyrrols externally.

The hemoglobin is oxygenated in the lungs (at high oxygen pressure) forming oxyhemoglobin. The oxygen is carried along the passageways—arteries, arterioles, capillaries (low oxygen pressure)—where it is freed from its loose combination with hemoglobin, and travels across the capillary walls and membranes to the tissues and the body cells. Then it passes back to the lungs to get more oxygen, and so on. The process is usually represented diagrammatically by the equation

$$Hb + O_2 \rightleftharpoons HbO_2$$

in which Hb represents hemoglobin and HbO_2 oxyhemoglobin.

The amount of oxygen that can be taken up per unit blood varies with the species and individual. Thus, according to Baldwin[65], the oxygen capacity per 100 cc blood is about 25 cc in mammals, 18.5 in birds, 12 in amphibia, 9 in reptiles and fishes. In animals which have the copper-containing hemocyanin* instead of the iron-containing hemoglobin, the O_2 capacity is only 2 to 8 cc oxygen per 100 cc blood. The metabolic rate of an animal is, of course, limited by the O_2 supply to the tissue, which in turn is limited by the circulation speed and the O_2 capacity of the blood.

There is a similar mechanism for removal of the CO_2 from the blood. On reaching the blood, the CO_2 combines to form $BHCO_3$, is carried to the lungs in association with the red cells, where H_2CO_3 is formed due to increased acidity consequent on formation of HbO_2, and is exhaled as CO_2. *Carbonic anhydrase*, a zinc-protein enzyme[66], associated with the red blood cells, catalyzes the cleavage of CO_2 from H_2CO_3 in the blood.

Hemoglobin splits into heme (or hemin, the chloride form), the non-protein part containing the iron-pyrrol complex, and globin, the protein part. Species differences are due to the differences in the protein part.

The structure of hemoglobin thus resembles that of enzymes in being an organic complex containing a protein and a prosthetic group. On removing the Fe from the heme, porphyrin[67] (hematoporphyrin, protoporphyrin) results; on removing the Mg from the corresponding chlorophyll group, porphyrin (aetioporphyrin) results.

It is interesting to contemplate the fact that chlorophyll, the green pigment in green plants, is structurally identical with hemoglobin, the red pigment in animals. They differ only in the central metal atom, chlorophyll containing magnesium instead of iron.

Another iron-containing respiratory pigment in aerobic cells, *cytochrome*, was elucidated chiefly by Keilin[68]. Cytochrome resembles hemoglobin in having the iron-porphyrin or heme group, but the heme is combined not with globin as in hemoglobin, but with pyridine[69], and the iron is not always in the divalent form, but it exists, alternately, in two forms—ferrous and ferric.

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[65] Baldwin, E., "An introduction to comparative biochemistry", Cambridge (England), 1937. See also Redfield, A. A., "The evolution of the respiratory function of the blood", *Quart. Rev. Biol.*, **8**, 31 (1933); "The hemocyanins", *Biol. Rev.*, **9**, 175 (1933).

* *Hemocyanin* is the copper-containing *blue* (when in oxygenated but colorless when in reduced form) respiratory blood pigment in certain cold-blooded animals, especially molluscs and crustaceans, corresponding to hemoglobin. Hemocyanin carries an atom of O per atom of Cu. Annelids have a green and also red respiratory pigments called, respectively, chlorocruorin and hemorythrin.

[66] Keilin, D., and Mann, T., "Carbonic anhydrase", *Nature*, **144**, 442 (1939).

[67] Cf. Dobriner, K., and Rhoads, C. P., "The porphyrins in health and disease", *Physiol. Rev.*, **20**, 416 (1940).

[68] Keilin, D., *Proc. Roy. Soc.*, **98B**, 312 (1925); **100B**, 139 (1926); **104B**, 206 (1929); **106B**, 418 (1930); Keilin, D., and Hill, R., *Id.*, **107B**, 286 (1930); *Erg. Enzymforsch.*, **2**, 239 (1933), and others.

In the presence of dehydrogenase, the metabolite is oxidized and the cytochrome reduced:

$$\text{metabolite} + \begin{matrix}\text{oxidized (colored)}\\ \text{cytochrome}\end{matrix} \xrightarrow{\text{dehydrogenase}} \begin{matrix}\text{oxidized}\\ \text{nutrients}\end{matrix} + \begin{matrix}\text{reduced (colorless)}\\ \text{cytochrome}\end{matrix}$$

In the presence of oxygen and cytochrome oxidase, the oxidized cytochrome is regenerated:

$$\begin{matrix}\text{Reduced (colorless)}\\ \text{cytochrome}\end{matrix} + O_2 \xrightarrow{\text{cytochrome oxidase}} \text{oxidized (colored) cytochrome}$$

The cytochrome is thus alternately reduced and oxidized, analogous to the way in which hemoglobin is alternately oxygenated and deoxygenated. The Fe in the cytochrome is oscillating between Fe^{++} and Fe^{+++}, transmitting electrons from H to O with the aid of cytochrome oxidase, while the Fe in hemoglobin is always in the ferrous form.

Cytochrome has been investigated in its oxidized and reduced forms most spectacularly in the bodies of insects. The scales of the insects were removed and observed under a microspectroscope. Typical 4-banded spectra appear under the spectroscope when the insect struggles and the cytochrome is reduced; the spectra disappear when the insect rests and the cytochrome is oxidized. Likewise in yeast, the spectrum appears when the air is reduced and disappears when air is supplied. In brief, the cytochrome is in the reduced form when the O_2 supply is poor, and in oxidized form when the O_2 supply is good.

The cytochrome complex was called by Warburg[70] "respiration catalyst" (*Atmungsferment*), the metal being considered the essential catalytic feature which "activates" the oxygen for oxidation. This reasoning is based on the spectacular effect of such chemically inert substances as cyanides on respiration. Cyanide causes almost instantaneous death by combining with the iron of the cytochrome and also with hemoglobin. Inhalation of HCN for only two seconds causes unconsciousness in six seconds and death in sixteen seconds. Other substances, as carbon monoxide, which combine readily with these respiratory carriers, have a similarly fatal effect. According to Warburg's old theory, cyanide *inactivates* the metal, the activator of the oxygen for oxidation.

Wieland[14], on the other hand, believed that the essential process is not oxygen activation but hydrogen activation by catalysts called dehydrogenases[15], and that the essential feature of oxidation is loss of hydrogen from the metabolite molecule, the oxygen acting as a relatively passive H acceptor. The carbon serves as the framework for the hydrogen. The essential overall reaction in biologic oxidation is accordingly

$$\text{Hydrogen} + \text{Oxygen} \rightarrow \text{Water}$$

Szent-Györgyi[35] believes that there is no contradiction between Wieland's and Warburg's theories, and that both O and H are activated.

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[69] Cf. Theorell, H., *Biochem. Z.*, **298**, 242 (1938).

[70] Warburg, O., *Science*, **61**, 575 (1925); **68**, 437 (1928); *Bull. Johns Hopkins Hospital*, **46**, 341 (1930).

Hemoglobin and cytochrome have many similarities: both have the same concentration of iron, both are quickly poisoned by cyanides, sulfides, and carbon monoxide. The difference between the two is that the iron atom changes valence ($Fe^{++} \rightleftharpoons Fe^{+++}$) in cytochrome but not in hemoglobin; hence the use of the term "oxidation" for cytochrome and "oxygenation" for hemoglobin. The molecular weight of cytochrome is of the order of 16.500 (assuming 1 Fe per mol of cytochrome), the weight formerly given for hemoglobin. It is now thought that the molecular weight of hemoglobin is about 68,000.

In view of the importance of iron in oxygenation and oxidation, it is evident that iron deficiency leads to serious metabolic disorders, structurally evidenced by *hypochromic* anemia (reduced hemoglobin formation). Like many other catalysts, however, iron is used over and over in the body. Therefore, it is only during growth, gestation, or in blood loss, in diarrhea, and intestinal disease, that considerable dietary iron is needed[71]. The dietary utilization of iron has been investigated[77] most spectacularly with the radioactive isotope Fe^{59}.

It is generally known that *iodine*[72] is the important inorganic element in thyroxine, a powerful oxidation accelerating hormone (Ch. 7).

There is no doubt that *copper* catalyzes iron utilization for hemoglobin formation[73] and that many oxidase enzymes (such as ascorbic acid oxidase, polyphenyl oxidase, cytochrome oxidase, catechol oxidase, tyrosinase, and laccase) contain copper, or are copper-protein oxidases[74].

Cobalt appears to be an essential trace element in the utilization of iron in sheep and cattle[75] but, apparently, not in rats.

Calcium[76], likewise, has a stimulating effect on some oxidases, as on succinic oxidase activity (bound up with cytochrome).

Just as hemoglobin and cytochrome contain iron,[77] so carbonic anhydrase (associated with the equilibrium between carbonic acid and carbon dioxide in their transportation by the blood) contains zinc. This was discovered by Keilin and Mann[78] and substantiated and extended by Hove *et al.*,[79] who previously demonstrated that zinc is a dietary essential[80].

Many other trace elements, such as Al, Be, B, Cr, Si, Sr, Sn, T, and Ni, are present in animal tissues[81], but their function, if any, is not understood. Thus vanadium[82] is regularly found in egg yolk and some tissues, but its function is not known. Bernheim[83], however, reported that vanadium stimulates oxidation of phospholipins in the presence of liver. Molybdenum may have some nutritional function[84].

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[71] Heath, C. W., *J. Am. Med. Assoc.*, **120,** 366 (1942).

[72] Salter, W. T., "Iodine", *Physiol. Rev.*, **20,** 345 (1940).

[73] Waddell, J., Elvehjem, C. A., Steenbock, H., and Hart, E. B., *J. Biol. Chem.*, **77,** 777 (1928); **84,** 115 (1929). Elvehjem, C. A., and Hart, E. B., *J. Nut.*, **19,** 207 (1940). Elvehjem, C. A., "The biological significance of copper", *Physiol. Rev.*, **15,** 471 (1935). Schultze, M. O., "Metallic elements and blood formation", *Id.*, **20,** 37 (1940). Robscheit-Robbins, F. S., and Whipple, G. H., *J. Exp. Med.*, **75,** 481 (1942).

[74] Tauber, H., *Ann. Rev. Biochem.*, **10,** 51 (1941).

[75] Lines, E. W., and Marston, H. R., *J. Council Sci. Ind. Res. Australia*, **8,** 111, 117 (1935). Neal, W. M., and Ahman, C. F., *J. Dairy Sci.*, **20,** 741 (1937).

[76] Axelrod, A. E., Swingle, K. F., and Elvehjem, C. A., *J. Biol. Chem.*, **140,** 931 (1941); **145,** 581 (1942).

[77] Whipple, G. H., *et al.*, *J. Exp. Med.*, **69,** 739 (1939); **76,** 15 (1942).

[78] Keilin, D., and Mann, T., "Carbonic anhydrase", *Nature*, **144,** 442 (1939); *Biochem. J.*, **34,** 1163 (1940).

[79] Hove, E., Elvehjem, C. A., and Hart, E. B., *J. Biol. Chem.*, **136,** 425 (1940).

[80] Todd, W. R., Elvehjem, C. A., and Hart, E. B., *Am. J. Physiol.*, **107,** 146 (1934).

[81] Calvery, H. O., *Food Research*, **7,** 313 (1940). Rusoff, L. L., Florida Agr. Exp. Sta. Bulls. 356 and 359, 1941.

Some trace elements are important in food, especially in dairy technology[85] (Sect. 6.3). Thus, tallowiness of sweetened condensed milk is attributed to catalytic oxidations by contact with copper and/or iron. Tallowy, oily, and fishy flavors of butter and ice cream are also attributed to such oxidations of the fats or phospholipids catalyzed by contact with copper and/or iron. Ice cream containing strawberries and related plant materials may develop off-flavors due to the catalytic oxidative action of the plant enzymes on the butterfat or on its phospholipids. The presence of iron (ferrous) in milk may destroy enough vitamin A to cause "salt ophthalmia" in animals fed $FeSO_4$ with their milk[86]. The low concentration of iron and copper in milk may be "explained" by the fact that their presence would be destructive to some vitamins.

Minerals have, of course, other functions, physicochemical[87] and structural[88]. Thus the skeleton contains about 85 per cent calcium phosphate, and in fact the total body ash contains about 75 per cent calcium phosphate. About 70 per cent of the body's phosphorus is in the skeleton. The phosphate is thus an extremely important structural as well as catalytic group.

6.4.3: Vitamins in biologic oxidations with special reference to the relation between vitamin B and bios. The vitamins are usually divided into fat-soluble and water-soluble categories[89].

Little is known about the catalytic significance in oxidoreductions of the fat-soluble vitamins. They are not universally distributed or needed. Cockroaches[90], for example, need no vitamin A; goats[91] need no vitamin E; yeasts need no vitamins A, E, D, or K.

The functions of the fat-soluble vitamins are rather more specialized than general oxidoreduction. Thus *vitamin A* is the prosthetic group of a very specialized conjugated protein system serving a visual function in higher animals. The equilibrium visual purple (rhodopsin) ⇌ visual yellow (retinene) ⇌ visual white in the retinal rods, involving also visual violet (iodopsin) in the retinal cones, is concerned with adjustment of vision to bright and dim light[92]. But riboflavin is also important in the vision mechanism, where it forms a "photo compound"[93], and in biological phosphorescence.

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[82] Daniel, E. P., and Hewston, E. M., *Am. J. Physiol.*, **136**, 772 (1942).

[83] Bernheim, F., *J. Biol. Chem.*, **127**, 353 (1939).

[84] Teresi, J. D., Elvehjem, C. A., and Hart, E. B., "Molybdenum in the nutrition of the rat", *Am. J. Physiol.*, **137**, 504 (1942).

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[87] Macallum, A. B., "Paleochemistry of body fluids", *Physiol. Rev.*, **6**, 316 (1926). Shohl, A. T., "Minerals in relation to acid base equilibrium", *Id.*, **3**, 509 (1923). Ringer, S., "Influence of body constituents on heart contraction", *J. Physiol.*, **4**, 29 (1883). Loeb, J., "Proteins and theory of colloid behavior", McGraw-Hill Book Co., 1924. Sherman, H. C., "Chemistry of food and nutrition", Macmillan, 1941.

[88] Shohl, A. T., "Mineral metabolism", Reinhold, 1939.

[89] Osborne, T. B., and Mendel, L. B., *J. Biol. Chem.*, **16**, 423 (1913) and **20**, 379 (1915). McCollum, E. V., and Davis, M., *Id.*, **15**, 167 (1913), and **23**, 181 (1915).

[90] Bowers, R. E., and McCay, C. M., *Science*, **92**, 291 (1940).

[91] Thomas, B. H., Cannon, C. Y., *et al.*, *J. Dairy Sci.*, **18**, 431 (1935); *J. Nut.*, **15**, Suppl. 10 (1938).

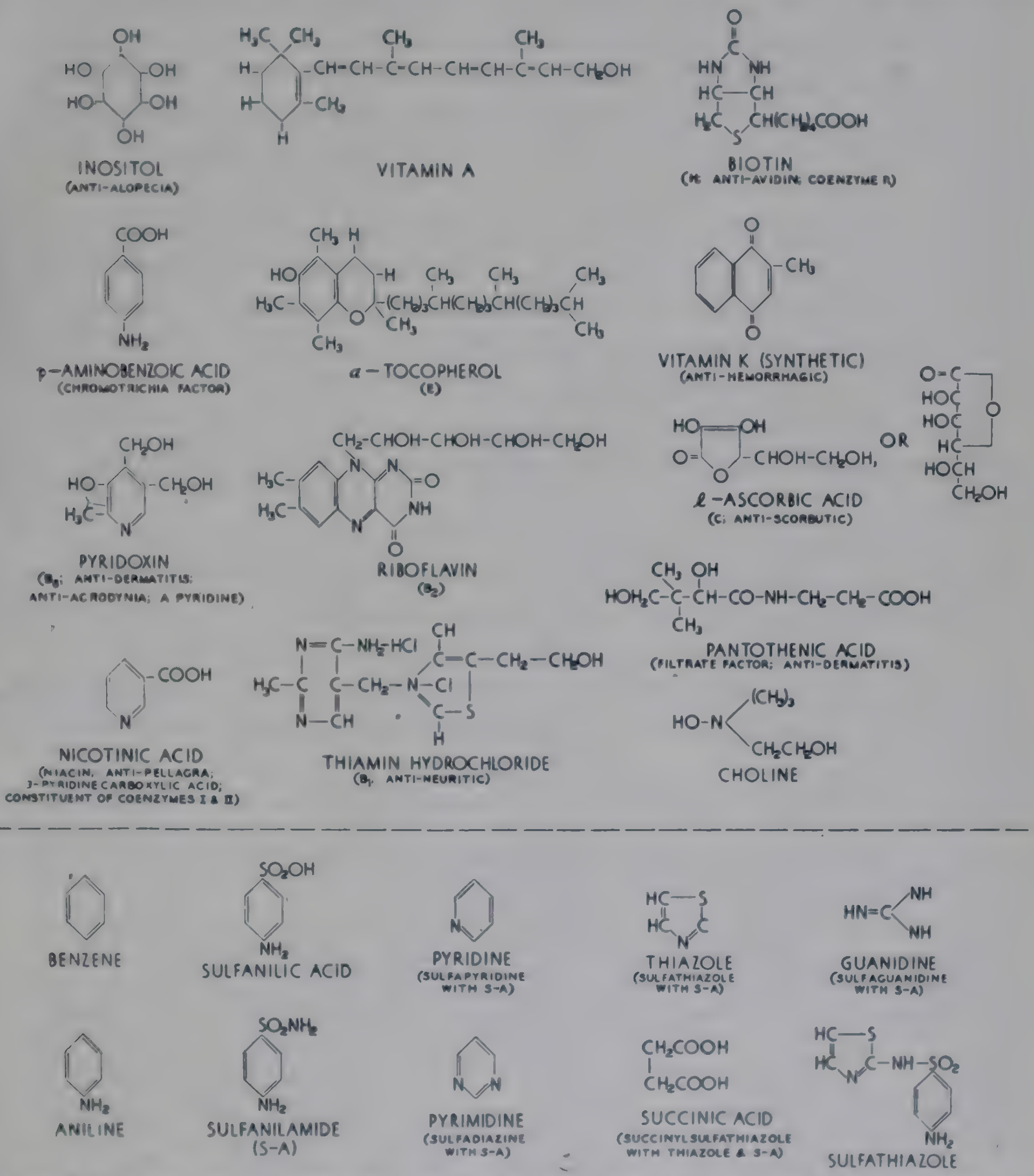

Fig. 6.2—Formulas of some vitamins and of some synthetic chemicals similar to vitamins which may "compete" with or "block" the vitamin in its relation to some essential enzyme system or action. See Sect. 7.1 for discussion of anti-vitamins and anti-hormones.

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[92] Wald, G., and Steven, D., *Proc. Nat. Acad. Sci.*, **25**, 344 (1939). For a review of Adams, Fredericia, Hecht, Wald, and others, see Isaacs, B. L., Jung, F. F., and Ivy, A. C., *J. Am. Med. Assn.*, **111**, 1771 (1938).

[93] Chase, A. M., *Science*, **85**, 184 (1937). Adler, E., and Euler, H., *Nature*, **141**, 790 (1938).

Vitamin A is apparently not a basic or general biocatalyst; nevertheless in some species its deficiency leads to widespread and grave symptoms. The vitamin A deficiency symptoms in humans are generally known. Vitamin A deficiency in growing cattle leads to constriction of the optic foramen with consequent optic nerve constriction and blindness; syncope likely produced by increased intracranial pressure; papillary edema and nyctalpia; bleaching of the tapetum lucidum of the retina, but not keratitis[94]; degeneration of germinal epithelium of the testes and absence of spermatozoa, and changes in the pituitary (T. S. Sutton); enteritis, kidney and liver lesions, and diarrhea[95].

Vitamin E (α-tocopherol[96]) may be a respiratory enzyme[97], but the most striking effects[98], in case of deficiency, are on the pituitary[99] and reproduction in general, leading to resorptive sterility and degeneration of the germinal epithelium in *rats*[99, 100], muscular dystrophy and paralysis in rats, guinea pigs and rabbits[101] and encephalomalacia in chicks[102] (Ch. 20).

Vitamin K, a quinoid[103], such as 2-methyl-1,4-naphthoquinone, may be an oxidation catalyst[104], but it is known only as being necessary for prothrombin formation. Prothrombin is, in fact, the proenzyme of thrombin, which converts fibrinogen to fibrin in blood clotting.

Vitamin D (irradiated ergosterol or 7-dehydrochloesterol[105]) is known for its catalysis of absorption of calcium and phosphates from the intestinal tracts, bone formation, and prevention and cure of rickets[106].

On the contrary, most of the water-soluble vitamins of the vitamin B or the bios type appear to be almost universally distributed and involved in basic oxidoreductions.

The story of the development of our knowledge of the interrelation between vitamin B and bios[107] is fascinating. About 1860 Pasteur[108] observed that yeast requires some factor for growth and fermentation which Wildier[109], in 1901, called *bios.* It is now known that bios is not a factor, but a family containing perhaps a dozen members, designated "growth factors". The important development emerged that the yeast "growth factors" are identical with a dozen-odd vitamins which make up what is now called the vitamin B complex. Nine of these factors have been obtained in crystalline form.

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[94] Moore, L. A., "Carotene and calf blindness", *J. Nut.*, **17**, 443 (1939). Wolbach, S. B., and Bessey, O. A., *Physiol. Rev.*, **22**, 233 (1942).

[95] Bechdel, S. I., *et al.*, *Am. J. Vet. Res.*, **3**, 27 (1942).

[96] Smith, L. I., *Chem. Rev.*, **27**, 287 (1940).

[97] Friedman, I., and Mattill, H. A., *Am. J. Physiol.*, **131**, 595 (1941).

[98] Mattill, H. A., *Ann. Rev. Biochem.*, **10**, 409 (1941).

[99] Wieske, B. P., and Bachrach, A. L., *Nature*, (Dec. 4, 1937) p. 943. Drummond, *et al.*, "Vitamin E: A Symposium", Heffer & Sons, 1939. Drummond, *et al.*, *Endocrinology*, **1**, 275 (1939). Biddulph, C., and Meyer, R. K., *Am. J. Physiol.*, **132**, 259 (1941).

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[101] Evans, H. M., and Burr, G. O., *J. Biol. Chem.*, **76**, 273 (1928). Goettsch, M., and Pappenheimer, A.M., J. Exp. Med., **54**, 145 (1931). Mackenzie, C. G., and McCollum, E. V., *J. Nut.*, **19**, 345 (1940); **21**, 225 (1941). Goettsch, M., and Ritzmann, J., *J. Nut.*, **17**, 371 (1939). Evans, H. M., *Id.*, **19**, 547 (1940).

[102] Pappenheimer and Goetsch, *J. Exp. Med.*, **53**, 11 (1931). Adamstone, F. B., *Arch. Path.*, **31**, 603 (1941).

[103] Fieser, L. F., "The chemistry of vitamin K", *Ann. Int. Med.*, **15**, 648 (1941).

[104] Bernheim, F., *J. Biol. Chem.*, **134**, 457 (1940).

[105] Bills, C. E., "The chemistry of vitamin D", *Physiol. Rev.*, **15**, 1 (1935).

[106] Mellanby, E., "Rickets", *J. Physiol.*, **52**, liii, liv (1919); *Lancet*, **1**, 407 (1939). McCollum, E. V., *et al.*, *J. Biol. Chem.*, **53**, 293 (1922).

The modern study of the B vitamins may be said to have begun[110] with the antiberiberi or antipolyneuritis factor, now called thiamine or vitamin B_1. About 1897 Eijkmann[111] observed that beriberi results from the lack of a substance present in rice polishings. In 1911 Funk[112] prepared the beriberi-curative substance from rice polishings; detecting an amine therein, he named the substance vitamin—a "vital amine". It was a charmed name which outlasted the accessory food substance and growth-factor designations employed by[113] Hopkins and by Osborne and Mendel.

Peters[114] observed that thiamine deficiency in the diet results in deficiency of cocarboxylase, the catalyst for splitting CO_2 from pyruvic acid with consequent accumulation of pyruvic acid, associated with the beriberi syndrome.

The function of thiamine is that of a prosthetic group in a respiratory enzyme. But, of course, like other vitamins, it also influences growth rates which are coupled with oxidoreductions; the early assay work for thiamine, as for other vitamins, was conducted by the growth method.

The knowledge of the B vitamins (needed by higher animals) thus parallelled the knowledge of bios or growth factors (needed by yeast and other plants). But it is only recently[115] that it has become definitely known that the two, bios and vitamin B, are identical. Yeast, liver, and rapidly growing plants are the best source of the B vitamins.

Note, however, the difference in the synthesizing powers of animals and

[107] Williams, R. J., *Biologic Reviews*, **16**, 49 (1941); *Enzymologia*, **1**, 387 (1941); Univ. Texas Publ. 4137, 1941. See also: Tanner, W. F., *Chem. Rev.*, **1**, 397 (1925); Miller, W. L., *J. Chem. Ed.*, **7**, 257 (1930); Peskett, G. L., *Biol. Rev.*, **8**, 1 (1933).

[108] Pasteur, L., "Memoire sur la fermentation alcoolique", *Ann. chim. Phys.*, **58**, 323 (1860); Pasteur, "Etudes sur la biere", Paris, 1876.

[109] Wildier, E., *La cellule*, **18**, 313 (1901).

[110] The earliest publication indicating that milk whey (free from casein, fat, sugar, and even ash) contains an indispensable dietary substance, what is now called vitamin B, is attributed to Lunin, G., *Z. physiol. Chem.*, **5**, 31 (1881).

[111] Eijkmann, C., *Virchow's Arch.*, **148**, 523 (1897).

[112] Funk, C., *J. Physiol.*, **43**, 395 (1911). Cf. Drummond, J. C., *Biochem. J.*, **14**, 660 (1920).

[113] Hopkins, F. G., *Analyst*, **31**, 385 (1906); *J. Physiol.*, **49**, 425 (1912). See also Hopkins and Neville, D., *Biochem. J.*, **7**, 96 (1913); Osborne, T. B., and Mendel, L. B., *J. Biol. Chem.*, **13**, 233 (1912).

[114] Peters, R. A., *Biochem. J.*, **30**, 2206 (1936); **31**, 2240 (1937); **32**, 2031 (1938); **33**, 1109 (1939). Ochoa, S., and Peters, R. A., *Biochem. J.*, **32**, 1510, 1938. Sherman, W. C., and Elvehjem, C. A., *Am. J. Physiol.*, **117**, 242 (1936). Thompson, R. H. S., and Johnson, R. E., *Biochem. J.*, **29**, 694 (1935).

[115] Williams, R. J.[107]

plants. Animals must obtain theirs from external sources, hence, by definition, they are *exogenous catalysts* to animals; yeast and other plants synthesize them, hence, by definition, they are enzymes or hormones, *endogenous catalysts*, to plants.

Many animals, especially ruminants (cattle, sheep), need B vitamins, yet do not need them. They require them for their metabolic processes, and their tissues cannot synthesize them; but their gastrointestinal flora produce them in great abundance. Cattle[116] certainly do not need thiamine[117] (B_1), riboflavin[118] (B_2), niacin[119], pantothenic acid[120], pyridoxine[121] (B_6), ascorbic acid,[122] and perhaps vitamin K, other than supplied by the rumen flora. Indeed, it is said that cow manure is very rich in the B vitamins; it is certainly the richest known source of biotin[123].

Prior to a certain age, when the rumen begins to function, calves apparently do need an external source of the B vitamins, normally obtained from milk[124].

As previously noted, primate and guinea pig must ingest ascorbic acid with the food—it is a real vitamin, an exogenous catalyst to these species; but other species investigated synthesize ascorbic acid in the body, perhaps in the liver[125] and elsewhere, in fact, ascorbic acid tends to be destroyed in the intestinal tract of some species, such as cattle[126]. It should be understood, however, that low vitality due to any cause, such as poor nutrition and advanced age, is associated with reduced vitamin C production in animals that normally produce it, in which case ascorbic acid administration is indicated[127].

All animals must have ascorbic acid, an indispensable hydrogen carrier[128],

$$l\text{-ascorbic acid} \underset{\text{2GSH}}{\overset{\substack{\text{ascorbic}\\ \text{oxidase}}}{\rightleftarrows}} \text{dehydroascorbic acid} + 2\text{H}$$

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[116] Burkholder, P. R., *Proc. Nat. Acad. Sci.*, **28**, 285 (1942).

[117] Bechdel, S. I., Eckles, C. H., and Palmer, L. S., *J. Dairy Sci.*, **9**, 409 (1926). McElroy, L. W., and Goss, H., *J. Biol. Chem.*, **130**, 437 (1939); *J. Nut.*, **21**, 163 (1941). Wegner, M. I., Booth, A. N., Elvehjem, C. A., and Hart, E. B., *Proc. Soc. Exp. Biol. Med.*, **45**, 769 (1940); **47**, 90 (1941). Bethke, R. M., *et al.*, *J. Nut.*, **21**, 85 (1941).

[118] McElroy and Goss[117] and *J. Nut.*, **20**, 527, 541 (1940). Wegner, *et al.*[117]

[119] Wegner, et al.[117], (1940). Winegar, A. H., Pearson, P. B., and Schmidt, H., *Science*, **91**, 508 (1940).

[120] McElroy and Goss,[117] (1939), and *J. Nut.*, **21**, 163, 405 (1941). Wegner, *et al.*[117]

[121] McElroy and Goss,[117] (1939). Wegner, et al.[117]

[122] Thurston, L. M., Eckles, C. H., and Palmer, L. S., *J. Dairy Sci.*, **9**, 37 (1926); **12**, 394 (1929). Huffman, C. F., *et al.*, *Id.*, **25**, 983 (1942).

[123] Williams, R. J.[107]

[124] Savage, E. S., and McCay, C. M., "The nutrition of calves", *J. Dairy Sci.*, **25**. 595 (1942).

[125] Hopkins, F. G., and Slater, B. R., *Biochem. J.*, **29**, 2803 (1935).

[126] Knight, C. A., *et al.*, *J. Dairy Sci.*, **24**, 567 (1941).

[127] Phillips, P. H., *et al.*, *J. Dairy Sci.*, **23**, 873 (1940); **24**, 153 (1941). Sutton, T. S., *et al.*, *J. Biol. Chem.*, **144**, 183 (1942).

[128] The reverse reaction [*cf.* Borsook, H., and Jeffreys, C. E. P., *Science*, **83**, 397 (1936). Hopkins, F. G., and Morgan, E. J., *Biochem. J.*, **30**, 1446 (1936)]:

$$\text{dehydroascorbic acid} + 2\text{GSH} \rightarrow \text{ascorbic acid} + \text{GSSG}$$

Glutathione is also said to protect ascorbic acid (reduced form) from autoxidation.

Why does not the guinea pig synthesize ascorbic acid? Because, says Szent-Györgyi[129], the guinea pig was evolved in the tropics, always surrounded by ascorbic acid-rich green herbage; survival did not depend on ascorbic-acid production. Therefore, in the course of evolution this species lost the ability to produce it, or did not have to develop it. The same argument is extended to primates, who cannot produce ascorbic acid: they originated in the tropics.

Only dogs, pigs, and primates were definitely shown to be dependent on dietary nicotonic acid. It appears that rats and chickens can synthesize nicotinic acid,[130] without the aid of gastrointestinal flora.[131]

It thus seems that there are species, and perhaps individual differences in vitamin requirements; one, but not another, for example, develops rickets under the same conditions of vitamin D and calcium supply. The same is true of other vitamins.

Moreover, there are interesting supplementary vitamin and substrate relations. Thus, as is generally known, vitamin D is most effective with a milk diet, which is the reason for fortifying milk with vitamin D. There are similar supplementary relations between vitamins. Thus biotin is practically without effect on yeast growth unless pyridoxine is simultaneously added to the culture medium.[132] Certain rat acrodynias are more easily cured if both unsaturated fat and pyridoxine are fed than if only one of them is fed.[133] Pyridoxine and the essential fatty acids (especially linoleic, arachidonic and linolenic) supplement each other.[134]

Some, but not other, species or individuals may perhaps possess alternate catalysts when the normal one is lacking, or be more sensitively receptive to a given catalyst or to its lack.

Thiamine and riboflavin supplement each other, as indicated by the enormous acceleration of urinary riboflavin loss on decreasing the thiamine intake.[135]

Vitamins have many extremely interesting supplementary, antagonistic, balancing and detoxifying effects.

Thus to cite a few examples, Holmes[136] reported that ascorbic acid, in doses from 250 to 500 mg per day, detoxifies the excessive production of histamine,

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[129] Szent-Györgyi, A. v., "On oxidation, fermentation, vitamins, health, and disease", The Abraham Flexner Lecture Series 6, Published for Vanderbilt University, by Williams & Wilkins, Baltimore, 1939.

[130] Dann, W. J., *J. Biol. Chem.*, **140,** 935; **141,** 803 (1941).

[131] Snell, E. E., and Quarrels, E., *J. Nut.*, **22,** 483 (1941).

[132] Snell, E. E., Eakin, R. E., and Williams, R. J., *J. Am. Chem. Soc.*, **62,** 175 (1940).

[133] Birch, T. W., *J. Biol. Chem.*, **124,** 775 (1938). Richardson, L. R., Hogan, A. G., and Itschner, K. F., "Vitamin B_6, pantothenic acid, and unsaturated fatty acids as they affect rat dermatitis", Univ. Missouri Agr. Exp. Sta. Res. Bull. 333, 1941.

[134] Salmon, W. D., *Proc. Am. Soc. Biol. Chem.*, *J. Biol. Chem.*, **140,** CIX (1941). Burr, G. O., *Proc. Fed. Am. Soc. Exp. Biol.*, **1,** 224 (1942).

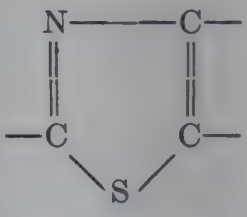
[135] Sure, B., and Ford, Z., *Proc. Fed. Am. Soc. Exp. Biol.*, **1,** 137 (1942); *J. Biol. Chem.*, **146,** 241 (1942).

[136] Holmes, H. N., and Alexander, W., *Science*, **96,** 497 (1942). See also Beyer, K. H., "Ascorbic acid inactivation in animals", *J. Pharm. Exp. Ther.*, **76,** 149 (1942).

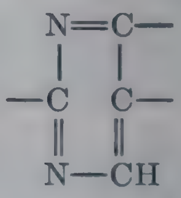
$C_5H_9N_2$, associated with hay fever, thereby relieving this ailment; Carratala[137] observed a detoxicating action of ascorbic acid in gold therapy; Levine[138] reported that vitamin C corrects in infants a disorder associated with excess ingestion of tyrosine and phenylalanine; feeding rice bran and yeast extracts tends to inhibit the development of certain types of cancer.[139] Fat synthesis in the body is dependent on the presence of all three vitamins—riboflavin, pyridoxine, and pantothenic acid[140]. The dietary need for biotin varies directly with the consumption of raw egg white (avidin) which binds the biotin, and there is an interesting interrelation between biotin, pimelic acid, and avidin (see below, p. 126). Raw fish has a substance which apparently similarly inactivates thiamine leading to "Chastek paralysis", a thiamine-deficiency syndrome resembling Wernicke's disease in man due to alcoholism.[141] The toxic effects of the sulfa drugs are antagonized or neutralized by thiamine and *p*-aminobenzoic acid[142, 143] (Fig. 6.2). Hyperthyroidism is relieved by vitamins C and A[144]. Methionine or choline and homocystine, detoxify pyridine[145], forming harmless methyl pyridinium hydroxide. Riboflavin often exerts a "sparing action" on thiamine[146], and so on. We shall presently note other supplementary relations, such as that of *p*-aminobenzoic acid and inositol; pyridoxine and fatty acid; choline and methionine.

There is a curious structural relation between thiamine (B_1), riboflavin (B_2), pyrodoxine (B_6), and nicotinic acid discussed above.

Williams employed the designation thiamine for vitamin B_1 because it contains a thiazole group.



But it also contains a pyrimidine or diazine group



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[137] Carratala, R. E., *J. Am. Med. Assn.*, **120,** 1331 (1942).

[138] Levine, S. Z., *et al.*, *J. Clin. Inv.* (March, 1941).

[139] Sugiura, K., and Rhoads, C. P., *Cancer Research*, **1,** 3 (1941).

[140] Steenbock, H., *et al.*, *J. Biol. Chem.*, **145,** 163 (1942).

[141] Green, R. G., Carlson, W. E., and Evans, C. A., *J. Nut.*, **21,** 243 (1941); *Am. J. Path.*, **18,** 79 (1942). Joliffe, N., *et al.*, *Arch. Neurol. Psychiat.*, **47,** 215 (1942).

[142] Elvehjem, C. A., *et al.*, *J. Biol. Chem.*, **145,** 137 (1942). Light, R. F., *et al.*, *J. Nut.*, **24,** 427 (1942).

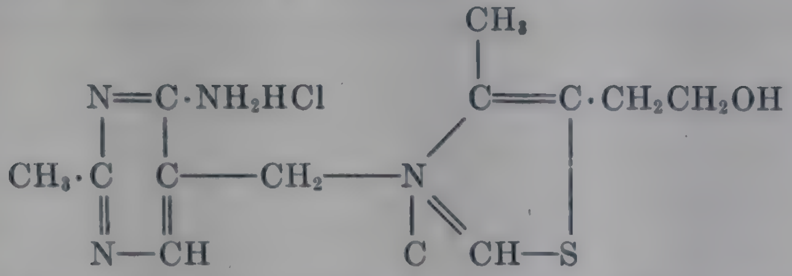
[143] West, R., *Proc. Soc. Exp. Biol. Med.*, **46,** 369 (1941). Wise, D., *J. Pharm. Exp. Ther.*, **76,** 156 (1942).

[144] Remington, R. E. *et al.*, *J. Nut.*, **24,** 597 (1942).

[145] Stekol, J. A., and Conway, W. J., Abst. Atlantic City Meeting Am. Chem. Soc. Sept. 1941, p. 13.

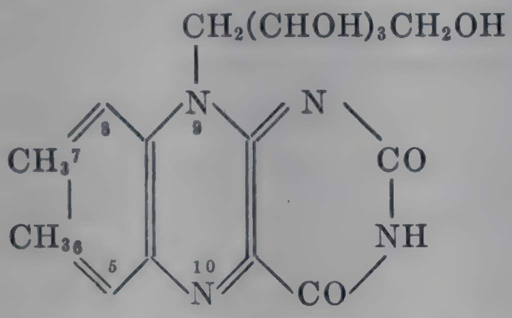
[146] Ellis, L. N., and Zmachinsky, A., *Science*, **86,** 245 (1937).

so that the formula of thiamine hydrochloride is



The relative functional importance of the two groups, thiazole and pyrimidine, is discussed by Lipmann.[165]

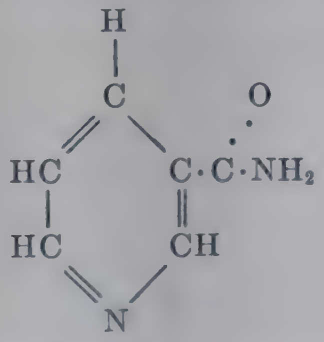
The interesting aspect from the viewpoint of unity in diversity is that riboflavin (vitamin B_2) also has a pyrimidine group. In this case, however, the pyrimidine group is coupled not to a thiazole, but it is a part of isoalloxazine, as indicated by the formula of *d*-riboflavin



A ribytyl group, $CH_2(CHOH)_3CH_2OH$, is attached to position 9; hence the name 6.7-dimethyl-9-*d*-ribytyl isoalloxazine.

This substance was apparently first observed by Szent-Györgyi[166] in his studies on biological oxidation-reduction systems (not vitamins). Szent-Györgyi called it *flave* and *cytoflave*.

Nicotinic acid (niacin), contains a closely related ring, not *pyrimidine*, but *pyridine*. Indeed, 3-pyridine-3-carboxylic acid amide



is the active antipellagra factor[167], when combined in the body with phosphoric acid, adenine and pentose (which together constitute cozymases I and II). Nicotinic acid has a —COOH group in place of —$CONH_2$.

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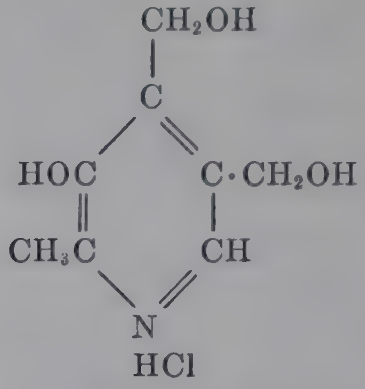
[165] Lipmann, F., *Nature*, **138**, 1097 (1936); *J. Am. Chem. Soc.*, **60**, 2674 (1938).

[166] Szent-Györgyi, A., and Banga, I., *Biochem. Z.*, **246**, 203 (1932).

[167] Elvehjem, C. A., Madden, R. J., Strong, F. M., and Woolley, D. W., "The isolation and identification of the anti-black tongue factor," *J. Biol. Chem.*, **123**, 137 (1938). Smith, D. T., Ruffin, J. M., and Smith, S. G., "Pellagra successfully treated with nicotinic acid," *J. Am. Med. Assn.*, **109**, 2054 (1937). Spies, T. D., Copper, C., and Blankenhorn, M. A., *Id.*, **110**, 622 (1938). Elvehjem, C. A., "Relation of nicotinic acid to pellagra," *Physiol. Rev.*, **20**, 249 (1940).

Pyridoxine (B_6) also contains a pyridine ring. Pyridoxine hydrochloride is 1-methyl-2-hydroxy-3-4-dihydroymethyl pyridine hydrochloride



This is an antidermatitis factor for rats[168] and a growth-stimulant for yeast[169], exised tomato roots[170], and so on. Unlike nicotinic acid, however, pyridoxine has not (yet) been shown to be a constituent of an enzyme, but it exists in nature as part of a protein complex, which may be the enzyme.

Pyridoxine deficiency may lead to convulsions[171] resembling epileptic fits in rats, pigs, and dogs. It is also needed by chicks. Pyridoxine appears to be a factor in hemoglobin formation and fatty acid utilization.[172]

It appears to be involved in protein metabolism and in the synthesis of fat from protein.[173]

We thus have two pyrimidine vitamins: thiamine (B_1) and riboflavin (B_2); and two pyridine vitamins: nicotinic acid and pyridoxine (B_6).

Coenzymes I and II are pyridine (nicotinic acid) derivatives, composed of one nicotinic acid, two pentoses (ribose), an adenine nucleotide, and two and three phosphoric acids, respectively. Hence the coenzymes I and II may be called di- and tri-phosphopyridine nucleotides, respectively.

phosphate-ribose-adenine nucleotide **niacin**
|
Coenzyme I: **phosphate-ribose-nicotinic acid** **enzyme**

The flavoprotein enzymes, such as Warburg's yellow enzyme, are structurally similar to the coenzymes I and II except that they have riboflavin, a pyrimidine group, instead of nicotinic acid, a pyridine group. The yellow enzyme, for example, is therefore diphosphopyrimidine nucleotide, just as cozymase I is diphosphopyridine nucleotide:

[168] Richardson, L. R., Hogan, A. G., and Itschner, K. F., "Vitamin B_6, pantothenic acid, and unsaturated acids as they affect dermatitis in rats," Univ. Missouri Agr. Exp. Sta. Res. Bull. 333, 1941. Lepkovsky, S., "Pyridoxine." Symposium Biological Action of Vitamins, Univ. Chicago Press, 1941.

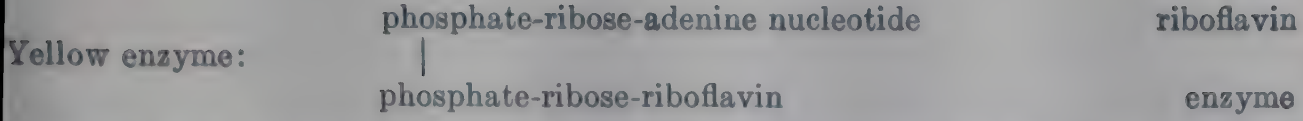
[169] Williams, R. J.[107], Möller, E. F., *Z. Physiol. Chem.*, **260**, 246 (1939).

[170] Robbins, W. J., and Schmidt, M. B., *Proc. Nat. Acad. Sci.*, **25**, 1 (1939).

[171] Chick, H., *et al.*, *Biochem. J.*, **34**, 595 (1940). Lepkovsky, S., Jukes, T. H., *et al.*, *J. Nut.*, **16**, 197 (1938); *Science*, **95**, 331 (1942). Vilter, R. W., *et al.*, *Nature*, **145**, 388 (1940) Lee, J. G., and Hogan, A. G., Univ. Mo. Agr. Exp. Sta. Res. Bull. 342, 1942.

[172] Birch, T. W., *J. Biol. Chem.*, **124**, 775 (1938). Richardson, Hogan, and Itschner[168].

[173] McHenry, E. W., and Gavin, G., *J. Biol. Chem.*, **138**, 471 (1941).



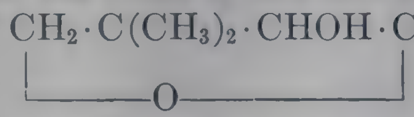
Yellow enzyme: phosphate-ribose-adenine nucleotide | phosphate-ribose-riboflavin — riboflavin enzyme

There is a striking difference between the amounts of different vitamin requirements in relation to body size. It appears that the need for the universally required vitamins of the vitamin B group, which are definitely participants in oxidations, such as thiamine, vary in proportion to energy metabolism, approximately in proportion to surface area; whereas the specialized vitamins, such as vitamin A, are probably needed in proportion to simple body weight.

When the energy-metabolism level is changed, the need for these oxidation vitamins is probably changed proportionately. This was reported by Mills and by György as regards the influence of change of temperature on thiamine and pyridoxine needs[174], by Drill and Overman as regards the influence of thyroid administration on pantothenic acid needs[175], and by the Pennsylvania Experiment Station[176] as regards the influence of exercise on thiamine need. Fever is known to increase the need for vitamin C.[177]

The numerical values for the vitamin requirements of different species and body weights cited in Chapter 20 bear out this statement as far as data are available.

The following are some of the more recently investigated vitamin or bios factors.



Pantothenic acid (name derived by R. J. Williams from the Greek meaning *from everywhere*, since it was found in most diverse living organisms), of which the lactone form is[178] $\underbrace{CH_2\cdot C(CH_3)_2\cdot CHOH\cdot CO}_{O}$, and the active form with β-alanine is $CH_2OH\cdot C(CH_3)_2\cdot CHOH\cdot CO\cdot NH\cdot CH_2\cdot CH_2\cdot COOH$, a component of the "filtrate factor"[179] (chick antidermatitis), is a growth-stimulant for yeast and perhaps for all microorganisms. It is a coenzyme in some fermentation processes.[180]

The *vitamin H* of György[181] and others was recently found to be identical with coenzyme R of Allison, Hoover, and Burk[182], identical with *biotin*, $C_{10}H_{16}O_3N_2S$, a urea-thienyl valeric-acid compound.[183]

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[174] Mills, C. A., *Am. J. Physiol.*, **133**, 525, 390 (1941). György, P., *J. Nut.*, **16**, 69 (1938).

[175] Drill, V. A., and Overman, R., *Am. J. Physiol.*, **135**, 474 (1942).

[176] Report Office of Experiment Stations, U. S. D. Agriculture for 1941, p. 71.

[177] Daum, K., *et al.*, *Proc. Soc. Exp. Biol. Med.*, **40**, 129 (1939).

[178] Williams, R. J., and Major, R. T., *Science*, **91**, 246 (1940).

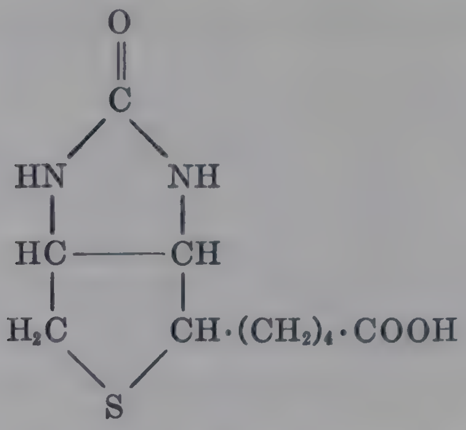
[179] Lepkovsky, S., and Jukes, T. H., *J. Biol. Chem.*, **114**, 109 (1936). Jukes, T. H., *J. Am. Chem. Soc.*, **61**, 975 (1939); *J. Biol. Chem.*, **129**, 225 (1939). Woolley, D. W., Waisman, H. A., and Elvehjem, C. A., *J. Biol. Chem.*, **129**, 673 (1939).

[180] Pratt, E. F., and Williams, R. J., "The effects of pantothenic acid on respiratory activity," *J. Gen. Physiol.*, **22**, 637 (1939).

[181] György, P., *et al.*, *Science*, **91**, 243 (1940); **92**, 609 (1940); **93**, 477 (1941). du Vigneaud, V., *et al.*, *Id.*, **92**, 62 (1940).

[182] Allison, F. E., Hoover, S. R., and Burk, D., *Id.*, **78**, 217 (1933).

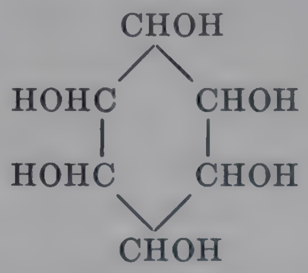
[183] du Vigneaud, V., *Id.*, **96**, 455 (1942).



Biotin, found in milk, egg yolk, liver, yeast, etc., increases respiratory metabolism in *Rhizobium*[182], fermentative and respiratory metabolism in yeast[184], protects rats[181] against the raw egg-white toxic factor[185], avidin[186], and chickens against perosis.[187] The superficial symptoms in the rat are eczematous dermatitis involving eyelids and lips and an ischemic gangrene of the tip of the tail.

A recent sensational observation is that biotin has a procarcinogenic effect on tumor formation induced by feeding the azo dye butter yellow to rats[188] and that riboflavin and related vitamins counteract the carcinogenic properties[189]. Like embryonic tissue, tumor tissue is richer in biotin than normal adult tissue[190, 191]. Pimelic acid may be a biotin precursor, and one is an accessory growth factor in the absence of the other[192].

Inositol, a hexahydroxycyclohexane,



widely distributed in biological material in the form of phosphoric ester, ("phytin" in plants, "muscle sugar" in animals) is a member of the bios complex[193] and is one of the antidermatitis and antialopecia vitamins[194]. However, the alopecia also develops in mice even in the presence of inositol if there is pantothenic acid deficiency[195]. It appears that mice can synthesize inositol if pantothenic acid is present[196]; the synthesis is perhaps accomplished by bacteria in the digestive tract.

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[184] Burk, D., Winzler, R. J., and du Vigneaud, V., Proc. Am. Soc. Biol. Chemists, 1941.

[185] Boas, M. A., *Biochem. J.*, **21,** 712 (1927). Parsons, H. T., and Kelly, E., *J. Biol. Chem.*, **100,** 645 (1933); *Biochem. J.*, **31,** 433 (1937).

[186] Eakin, R. E., Snell, E. E., and Williams, R. J., *J. Biol. Chem.*, **136,** 801 (1940); **140,** 535 (1941). György, P., *et al.*, *Science*, **93,** 477 (1941).

[187] Richardson, L. R., Hogan, A. G., and Miller, O. N., "Relation of biotin to perosis," Univ. Missouri Agr. Exp. Sta. Res. Bull. 343, 1942. Hegsted, D. M., *et al.*, *J. Nut.*, **20,** 599 (1940); **23,** 175 (1942). Jukes, T. H., and Bird, F. H., *Proc. Soc. Exp. Biol. Med.*, **49,** 231 (1942).

[188] du Vigneaud, V., *et al.*, *Science*, **95,** 174 (1942). See also *J. Am. Med. Assn.*, **118,** 982 (1942).

[189] Rhoads, C. P., *et al.*, *Science*, **93,** (1941); *Cancer Res.*, **1,** 3 (1941).

[190] West, P. M., and Waglom, W. H., *Science*, **93,** 525 (1941).

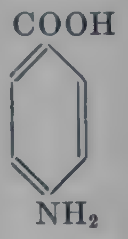
[191] Laurence, W. L., *Id.*, **94,** 88 (1941).

[192] du Vigneaud. V., Barbara Long, *et al.*, *Science*, **96,** (1942). Eakin, R. E., and E. A., *Id.*, p. 188.

Inositol deficiency may lead to the "biotin type" of fatty liver in the rat[197] or, like lipocaic, it appears to prevent the "biotin type" of fatty liver but not the "thiamine type".

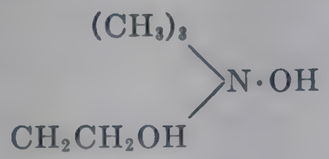
There is a curious relation between inositol and *p*-aminobenzoic acid; addition of *p*-aminobenzoic acid often precipitates the inositol-deficiency syndrome, and *vice versa*, causing a graying of hair in black rats similar to the graying due to pantothenic acid deficiency[198].

p-Aminobenzoic acid,



a member of the bios complex[199], was announced by Ansbacher[200] to be an "anti-gray hair factor" for black rats fed under certain conditions. It is said that it is not the absolute amount of *p*-aminobenzoic acid that is important in this syndrome, but its ratio to pantothenic acid, which controls the growth of the vitamin-synthesizing powers of the gastrointestinal flora[201]. Sure[202] reported that it may be a factor in fertility and lactation in the rat. It affects tyrosinase activity[203].

Choline, a trimethyl hydroxyethyl ammonium hydroxide,



$$\begin{matrix}(CH_3)_3 & \\ & \rangle N\cdot OH \\ CH_2CH_2OH & \end{matrix}$$

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[193] Eastcott, E. V., *J. Phys. Chem.*, **32,** 1094 (1928).

[194] Woolley, D. W., *J. Biol. Chem.*, **136,** 113 (1940); *Science*, **92,** 384 (1940).

[195] Woolley, D. W., *Proc. Soc. Exp. Biol. Med.*, **46,** 565 (1941).

[196] Woolley, D. W., *J. Exp. Med.*, **75,** 277 (1942).

[197] Gavin, G., and McHenry, E. W., *J. Biol. Chem.*, **139,** 485 (1941); *Proc. Fed. Am. Soc. Exp. Biol.*, **1,** 124 (1942).

[198] Wisansky, W. A., Martin, G. J., and Ansbacher, S., *J. Am. Chem. Soc.*, **63,** 1771 (1941).

[199] Rubbo, S. D., and Gillespie, J. M., *Nature*, **146,** 838 (1940).

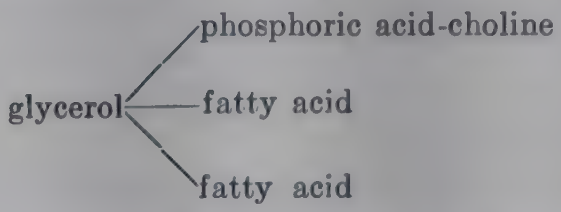
[200] Ansbacher, S., *Science*, **93,** 164 (1941). Martin, G., and Ansbacher, S., *J. Biol. Chem.*, **138,** 441 (1941); *Proc. Soc. Exp. Biol. Med.*, **48,** 118 (1941); *Proc. Fed. Am. Soc. Exp. Biol.*, **1,** 98 (1942).

[201] Martin, G. J., *Proc. Am. Soc. Exp. Biol.*, **1,** 58 (1942); *Am. J. Physiol.*, **136,** 124 (1942).

[202] Sure, B., *J. Nut.*, **22,** 499 (1941).

[203] Ansbacher, S., *et al.*, *J. Am. Chem. Soc.*, **63,** 1771 (1941).

closely related to acetylcholine, is a component of the phospholipid lecithin,



is often thought of as a vitamin[204], sometimes as a bios or growth factor since it is required by some bacteria and as a member of the B-vitamin complex[205]. However, growing rats can synthesize choline[206] (see below). It is mostly known for its catalysis of lipid phosphorylation (formation of phospholipid) and transport and oxidation[207]. Lack of dietary choline (or lecithin, or certain other methyl-containing groups), however, leads to diverse syndromes, such as perosis in chicks[208], impairment of lactation[209] (rats), fatty livers[207,210], hemorrhagic renal lesions[211], deficient vagus function (inadequate acetocholine formation)[212].

The body is apparently able to synthesize choline provided that the diet contains "labile methyl" groups[213, 214, 215], such as are present in methionine and betaine. Indeed, it appears that it is not choline that is the important factor but methyl groups in utilizable form for transmethylation (specific transfer of methyl groups as needed) and that the methyl groups of choline, methionine, and betaine are thus transferable.

From the above discussions it appears that choline is a "vitamin" in the special sense that it supplies indispensable methyl groups if the diet is inadequate in methionine (below 0.8 per cent methionine; or if casein is the sole source of protein, less than 30 per cent casein in the diet). Increasing cystine in the diet, or increasing food intake of any kind, increases the choline requirement[216]. High-fat and low-protein diets similarly increase the choline requirements, which if not satisfied may lead to cirrhosis of the liver[217].

6.5: Note on biologic synthesis with special reference to CO_2 assimilation

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[204] Best, C. H., *et al.*, *J. Physiol.*, **86,** 315 (1936). György, P., *Ann. Rev. Biochem.*, **11,** 309 (1942).

[205] King, C. G., *Ann. Rev. Biochem.*, **8,** 389 (1939).

[206] Jacobi, H. P., *J. Biol. Chem.*, **138,** 571 (1941).

[207] Welch, A. D., *Proc. Soc. Exp. Biol. Med.*, **35,** 107 (1936); **39,** 7 (1938) Chaikoff, I. L., *J. Biol. Chem.*, **127,** 211 (1939), and others.

[208] Jukes, T. H., *J. Nut.*, **20,** 445 (1940). Jukes and Almquist[58].

[209] Sure, B., *Id.*, **19,** 71 (1940).

[210] Best, C. H., Hershey, J. M., and Huntsman, M. E., *Am. J. Physiol.*, **101,** 7 (1932). Best, C. H., and Ridout, J. H., *Ann. Rev. Biochem.*, **8,** 349 (1939). Best, C. H., *Science*, **94,** 523 (1941).

[211] Griffith, W. H., *J. Nut.*, **19,** 437 (1940); **21,** 291, 633 (1941); **22,** 239 (1941).

[212] Solandt, D. Y., and Best, C. H., *Nature*, **144,** 376 (1939).

[213] Stetten, D., *J. Biol. Chem.*, **140,** 143 (1941).

[214] du Vigneaud, V., *et al.*, *J. Biol. Chem.*, **134,** 787 (1940); **140,** 625 (1941).

[215] du Vigneaud, V., *et al.*, *J. Biol. Chem.*, **131,** 57 (1939); **134,** 787 (1940); **139,** 917 (1941); **140,** 625 (1941), and other papers.

[216] Griffith, W. H., and Mulford, D. J., *J. Am. Chem. Soc.*, **63,** 929 (1941); *J. Nut.*, **23,** 91 (1942).

[217] Blumberg, H., *et al.*, *Science*, **93,** 598 (1941); *Proc. Fed. Am. Soc. Exp. Biol.*, **1,** 187 (1942).

in heterotrophs. Anabolism, or biologic synthesis, is necessarily coupled with catabolism, or biologic oxidation, discussed in the preceding sections, and some of the same oxidoreduction catalysts involved in catabolism are also involved in anabolism. This section presents a few examples of biologic synthesis beginning with a brief footnote, by way of reference to the literature, on the assimilation of CO_2-carbon by heterotrophs.

Winogradsky[218] discovered in 1890 that some soil organisms obtain energy by oxidation of ammonia to nitrites, and nitrites to nitrates, and using this energy for carboxylation, that is, assimilation of carbon from atmospheric CO_2, independently of radiant energy, for building up their tissues (Ch. **2**).

The new development is that saprophytic bacteria and certain tissues of warm-blooded animals thought to be able to utilize only complex organic substances (carbohydrates, fats, proteins, and their close derivatives) have been observed to utilize CO_2. These investigations have been greatly aided by the use of isotopes—heavy carbon, C^{13}, and radioactive carbon, C^{11}—as tracers.

The literature, adequately reviewed[219], indicates three paths of investigation. First is the fixation of CO_2 in urea formation by the liver. This was demonstrated by Krebs[220] in 1932, confirmed by Rittenberg[221], using C^{13}, and Evans[222], using C^{11}.

Second is the utilization of CO_2 in heterotrophic bacteria, discovered by Wood and Werkman[223] in 1935 and adequately confirmed[224] on propionic acid bacteria.

Third, Evans and Slotin[225] discovered and Wood and Werkman[226] confirmed the utilization of CO_2 by pigeon-liver tissue; the latter showed that the CO_2 carbon appeared in the α-ketoglutaric acid and other acids[227]. Wood and Werkman[228] proposed the following equation to represent the assimilation of tagged C into succinic acid (if such occurs), indicating that the carbon is fixed in the carbonyl group adjacent to the methylene.

$$C^{13}O_2 + CH_3COCOOH \rightarrow C^{13}OOHCH_2COCOOH \xrightarrow{+4H} C^{13}OOHCH_2CH_2COOH + H_2O$$

It appears that CO_2 may also be utilized by intact higher animals. $C^{11}O_2$ was administered in the form of $NaHC^{11}O_3$ and the C^{11} was found in the newly formed liver glycogen[229].

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[218] Winogradsky, S., *Ann. Inst. Pasteur*, **4,** 213 (1890); **5,** 92, 577 (1891).

[219] Van Niel, C. B., *Ann. Rev. Biochem.*, **6,** 607–8 (1937). Cori, C. F., and G. T., *Id.*, **10,** 157 (1941). Ball, E. G., *Id.*, **11,** 1 (1942). Werkman, C. H., and Wood, H. G., *Adv. Enzymology*, **2,** 135 (1942); *Bot. Rev.*, **8,** 1 (1942). Evans, E. A., Jr., *Science*, **96,** 25 (1942).

[220] Krebs, H. A., *Z. physiol. Chem.*, **210,** 33 (1932).

[221] Rittenberg, D., and Waebch, H., *Id.*, **136,** 799 (1940).

[222] Evans, E. A., and Slotin, L., *J. Biol. Chem.*, **136,** 805 (1940).

[223] Wood, H. G., and Werkman, C. H., *J. Bact.*, **30,** 332 (1935); *Biochem. J.*, **30,** 48 (1936).

[224] Wood, H. G., and Werkman, C. H., *J. Biol. Chem.*, **135,** 789 (1940); **139,** 365 (1941).

[225] Evans, E. A., and Slotin, L., *J. Biol. Chem.*, **136,** 301 (1940).

[226] Wood, H. G., and Werkman, C. H., *Id.*, **139,** 483 (1941); **142,** 31 (1942).

[227] Evans, E. A., *Id.*, **141,** 439 (1941); *Science.*[219]

[228] Wood, H. G., and Werkman, C. H., *Biochem. J.*, **30,** 48 (1936); **32,** 1262 (1938).

[229] Solomon, A. K., Vennesland, B., Klemperer, F. W., Buchanan, J. M., and Hastings, A. B., *J. Biol. Chem.*, **140,** 171 (1941). Conant, J. B., *et al.*, *Id.* **137,** 557 (1941).

In this connection a note may be in order concerning the photosynthetic assimilation of CO_2. Photosynthesis appears[230] to occur in two stages, (1) CO_2 fixation and (2) utilization of radiant energy for activating the fixation process. The first step appears to occur (but perhaps not in similar manner) in both autotrophs and heterotrophs but, of course, not the utilization of radiant energy in heterotrophs.

In photosynthesis, H_2O is the H-donor and CO_2 is the H-acceptor. As the potential difference between the two is 1.2 to 1.3 volts[231], "the wrong side" by about 56 Cal per equivalent, it follows that at least 56 Cal per equivalent, or about 670 Cal (56 x 6) per mol hexose, is expended for the formation of hexose. Chlorophyll is perhaps the hydrogen carrier in the dehydrogenation of H_2O.

All the fermentation and oxidation processes, such as:

$$\text{glycogen} \longrightarrow \text{glucose} \longrightarrow \text{triose} \longrightarrow \text{glyceraldehyde} \longrightarrow \text{pyruvic acid} \longrightarrow \text{lactic acid}$$

and so on, are, of course, based on previous syntheses. The study of the synthesis, experimental and theoretic (thermodynamic), is in the initial stage, although there is an immense literature on the subject, for heterotrophs[232] as well as for autotrophs.

It may be appropriate to mention an illustration of the reversal of the decarboxylation catalyzed by vitamin B_1, or rather by thiamine pyrophosphate or cocarboxylase. The decarboxylation reaction cited was

$$\underset{\textit{pyruvic acid}}{CH_3 \cdot CO \cdot COOH} \rightarrow \underset{\textit{acetaldehyde}}{CH_3 \cdot CHO} + CO_2$$

Now it is believed that thiamine pyrophosphate similarly catalyzes the reverse process in heterotrophs, namely carboxylation[232–234]. The process is assumed to be associated with various theoretical "cycles" sponsored by different investigators as, for example, the "citric acid cycle"[235] or the "succinic acid cycle"[236], all beginning with a carboxylation reaction, usually carboxylation of pyruvic acid, under the influence of various catalysts, of which carboxylase is one.

There is a great deal of discussion in the literature concerning another type of synthesis, namely that of glycogen from lactic acid.

Though the idea has not generally been accepted[237], Meyerhof[238] suggested that about 25 per cent of the lactic acid formed during intense muscular work is completely oxidized during the recovery period, and the energy therefrom converts the remaining 75 per cent of the lactic acid to glucose or glycogen. The synthesis of glucose from lactic acid in muscle, and especially in the liver, was demonstrated long ago[239]. As in the glycolysis of glucose to lactic acid so in the reverse process, the first stage is phosphorylation, and the first product is phosphorpyruvic acid formed from lactic acid[240].

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[230] Ruben, S., *et al.*, *J. Am. Chem. Soc.*, **62,** 3443, 3450, 3451 (1940), *Science*, **90,** 570 (1939).

[231] Van Niel, C. B., *Cold Spring Harbor Symposia on Quantitative Biology*, **3,** 138 (1935); *Ann. Rev. Biochem.*, **6,** 607–8 (1937).

[232] See Werkman and Wood[219].

[233] Wood, H. G., and Werkman, C. H., *Biochem. J.*, **32,** 1262 (1938); **34,** 7 (1940).

[234] Krebs, H. A., and Eggleston, L. V., *Id.*, **34,** 442, 460, 1234, 1383 (1940).

[235] Krebs, H. A., and Johnson, W. A., *Enzymologia*, **4,** 148 (1937).

[236] Laki, K., Straub, F. B., and Szent-Györyi, A., *Z. physiol. Chem.*, **247,** 1 (1937).

[237] Margaria, Edwards, and Dill,[28] Sacks and Sacks[27].

[238] Meyerhof, O., *Arch. Ges. Physiol.*, **185,** 11 (1920). Hill, A. V., *Physiol. Rev.*, **2,** 329 (1922).

In addition to Meyerhof's theory[241] of the synthesis of glucose from lactic acid, others have been suggested[242]. Tentative data and theories are also available[243] on the formation of triose from phosphoglyceric acid, glucose from triose, and glycogen from glucose. Similarly, tentative data and theories are available for reductive amination processes, that is, synthesis of amino acids from intermediate carbohydrate-metabolism products[244], as for the oxidative deamination processes (Sect. 20.7).

The reaction

$$\underset{(\textit{alanine})}{CH_3\cdot CHNH_2\cdot COOH} \rightleftharpoons \underset{(\textit{pyruvic acid})}{CH_3\cdot CO\cdot COOH} + NH_4^+ + 2H^+ + 2e$$

is reversible[245]. Thus glycolysis (in the presence of ammonia) may thus yield alanine instead of lactic acid.

6.6: Summary and appendix. A brief discussion is presented of some of the mechanisms of biologic oxidation or dissimilation or catabolism, and of synthesis or assimilation or anabolism. Some of the water-soluble vitamin are involved in all biologic oxidation, ranging from bacteria to man; the fat-soluble vitamins, on the other hand, appear to be involved in special processes found only in higher animals.

Biologic oxidation is a stepwise process involving many intermediate steps and catalysts, as indicated diagrammatically:

$$\text{glucose} \rightarrow \text{hexose phosphate} \rightarrow \text{intermediate compounds} \rightarrow H_2O + CO_2$$

phosphorylation catalysts and donors, such as phosphorylases and adenylic pyrophosphate	pyridinoprotein enzymes flavoprotein enzymes iron-porphyrin enzymes cytochromes cytochromes oxidases, etc., involving vitamins and inorganic groups.	carboxylase and cocarboxylase (vitamin B_1)

The oxidation consists in elaborate, stepwise, transfer of electrons from the electron donors (substrates) to electron acceptors. The ultimate electron acceptor in aerobic oxidation is atmospheric oxygen; but in fermentation the acceptor may be formed by the electron donor. A central feature of biologic oxidations is that they are coupled with phosphorylation of the carbonyl groups of the substrate, forming various intermediate phosphate esters.

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[239] Embden, G., *et al.*, *Z. Physiol. Chem.*, **88,** 210 (1913). Meyerhof, O., *Arch. ges. Physiol.*, **182,** 284 (1920). Lundsgaard, E., *et al.*, *Skand. Arch. Physiol.*, **73,** 296 (1936).

[240] Ferdman, D. L., and Epstein, S. F., *Science*, **91,** 365 (1940).

[241] Meyerhof, O., *et al.*, *Biochem. Z.*, **297,** 113 (1938). Green, D. E., Needham, D. M., and Dewan, J., *J. Biochem.* **31,** 2327 (1937).

[242] Kluyver, A. J., *Arch. Mikrobiol.*, **2,** 245 (1931). Conant, J. B., and Tongberg, C. O., *J. Biol. Chem.*, **88,** 701 (1930). Hastings, A. B., *et al.*, *Science*, **91,** 421 (1940).

[243] See Kalckar's review, 1941[16].

[244] Adler, E., *et al.*, *Biochem. J.*, **33,** 1028 (1939).

[245] Wurmser, R., *Compt. Rend. Soc. Biol.*, **128,** 133 (1938).

The following is a list of definitions of the vitamins, minerals, and their associated enzymes. The nutritional aspects of vitamins are discussed in Sections 20.5 and 20.6. See Section 7.8.3 for vitamins and hormones in green plants.

I. B vitamins or bios

1. *Thiamine*, vitamin B_1, antineuritic factor: Eijkman 1893, Funk 1911; crystallized by Jansen & Donath, 1926; $C_{12}H_{17}ON_4SCl \cdot HCl$ (Windaus 1931); a thiazole pyrimidine synthesized by Williams, 1936. It exists in the organism in the free form and as component of carboxylase and of cocarboxylase, a thiamine phosphoric ester (Lohmann and Schuster 1937) catalyzing the decarboxylation of pyruvic acid to acetaldehyde and CO_2 and also, carboxylation in the assimilation of CO_2.
2. *Riboflavin*, *lactoflavin*, vitamin B_2: $C_{17}H_2O,N_4O_6$, (Kuhn, et al., 1934); an isoalloxazine (Kuhn & Karrer, 1935), containing a pyrimidine ring. Exists as: (A) free riboflavin; (B) "coenzyme": (a) riboflavin-phosphate mono-nucleotide and (b) riboflavin-adenine-dinucleotide; (C) flavoprotein, which is the "coenzyme" in combination with protein. The free riboflavin is available to animals after phosphorylation. Milk contains the riboflavin mostly in the free and coenzyme forms, where it is called lactoflavin (Laki, 1933) and cytoflave (Banga and Szent-Györgyi, 1932). But egg, liver, yeast, young vegetation, and all rapidly-growing things are rich in it. The blue *B. pyacyaneous* color, which disappears on removal of air, indicates its reversible hydrogen-donating and accepting (carrier) functions. The riboflavin protein enzymes (hydrogen carriers) are exemplified by the "yellow enzyme" of Warburg and Christian, 1932, a mononucleotide; *d*-amino oxidase and diamine oxidase, dinucleotides; the diphorases, dinucleotides; xanthin oxidase, glucose oxidase, cytochrome-*c* reductase, mononucleotides, and so on.

   While the most conspicuous symptom of thiamine deficiency is nerve disease, that of riboflavin deficiency is skin (including eye, hair— alopecia—, etc.) disease, resembling vitamin A deficiency, leading to visual disturbance (often cataract, corneal opacity or keratitis) pellagra-like dermatitis, cheilosis (see under pyridoxine), scaly desquamation, inflammation of tongue, and so on. However, riboflavin deficiency also results in serious neuropathologic conditions[246].
3. *Nicotinic acid*, *nicotinamide*, niacin, PP (pellagra-preventing), G[247], $C_6H_5O_2N$ or $C_6H_5ON_2$, pyridine-3-carboxylic acid: found in rice polishings by Funk (1912), who also thought that pellagra is a nutritional disease, but he did not connect nicotinic acid deficiency with pellagra. This was done a quarter century later (1937–8) by Elvehjem, *et al.*, for blacktongue in dogs and by Lepkowsky, Jukes, *et al.*, on man.

   This vitamin exists in the form of two coenzymes (or coferments, or cozymases, or codehydrogenases, or coreductases), coenzyme I, diphophosphopyridine nucleotide, and coenzyme II, triphosphopyridine nucleotide (Warburg and Christian, 1935). As for riboflavin coenzymes, the nicotinamide enzymes may exist in combination with proteins; and as riboflavin enzymes, the nicotinamide enzymes are hydrogen carriers. In fact the hydrogen or electron is passed from the pyridine enzymes to the flavin enzymes. Coenzyme I catalyzes the equilibria, lactate ⇌ pyruvate, B-hydroxybutyrate ⇌ acetoacetate, alcohol ⇌ acetaldehyde, and so on; coenzyme II catalyzes the equilibria, citrate ⇌ α-keto-glutarate, glucose-6-phosphate ⇌ 6-phospho-gluconate, and so on.

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[246] Shaw, J. H., and Phillips, P. H., *J. Nut.*, **22**, 345 (1941).

[247] G, after J. Goldberger, the pioneer investigator. See *Public Health Reports*, **30**, 3117 (1915), and many papers thereafter.

The clinical symptoms are typical skin afflictions, mental confusion, and diarrhea.

. *Pyridoxine*, vitamin B_6, $C_8H_{11}O_3N$ (Kuhn, 1938): a pyridine compound (1-methyl-2-hydroxy-3-4-dihydroxymethyl pyridine, Kuhn and others, 1939), apparently exists in the body in the form of pyridoxine-protein. The symptoms of pyridoxine deficiency in the *rat*, is a dermatitis or acrodynia, similar to pellagra in man or blacktongue in dogs; also hypochromic anemia. Goldberger and Lillie, 1926, designated rat acrodynia factor; Chick, 1930, called it the Y factor; Richardson and Hogan, 1936, called it vitamin H; Lepkowsky, 1936, called it the I factor; György, 1939, called it pyridoxine and vitamin B_6, which name has been generally adopted. Pyridoxine appears to cure "cheilosis", formerly believed to be due to ariboflavinosis. Pyridoxine and nicotinic acid appear to be related functionally as well as structurally.

Both thiamine and pyridoxine are involved in the synthesis of fat from protein[248].

5. *Pantothenic acid*, $C_9H_{17}O_5N$, [the commercially available salt is $Ca(C_9H_{16}NO_5)_2$] a dimethyl butyryl amide (R. J. Williams *et al.*, 1939): an antidermatitis factor for chicks (many workers, especially Jukes, 1939, and Elvehjem *et al.*, 1939), growth stimulator, etc.
6. *Biotin*, coenzyme R, anti-avidin, or anti-egg-white injury factor, antiperosis factor, vitamin H of György, isolated and named by Kögl, 1935, $C_{10}H_{16}O_3N_2S$, a urea-thienyl valeric acid compound (du Vigneaud, György, *et al.*, 1940–2): Biotin deficiency in rats is recognized by the "spectacle eye" syndrome, and dermatitis in chicks, and other lesions.
7. *Inositol*, $C_6H_{12}O_6$, hexahydroxycyclohexane (Eastcott, 1928), a carbohydrate derivative. It is an antialopecia factor (Woolley, 1940), very widely distributed. It is a lipotropic factor (Gavin and McHenry, 1941).
8. *p-Amino benzoic acid*, $C_7H_7O_2N$, antiachromatricia factor for black rats (Ansbacher, 1941): very widely distributed in biologic material.
9. *Choline*, lipotropic factor (Best *et al.*, 1932): the methyl group is its essential component. Like betaine, choline has 3 methyl groups. The amino acid methionine, $CH_3 \cdot S \cdot (CH_2)_2 \cdot CHNH_2 \cdot COOH$, also has a methyl group; hence these three substances can be substituted for each other. Deficiency of the methyl grouping leads to "fatty livers", cirrhosis of the liver, hemorrhagic kidney degeneration, disturbance of lactation and growth, and paralysis of the suckling young.
10. Many more members are suspected in the B-complex family, and some have been proved to be present; but the chemical constitution of these has not yet been worked out. To avoid confusion, only three of the best known of these factors are cited. First is vitamin B_c, or the chick antianemia vitamin discovered and crystallized from aqueous liver extract by Hogan and associates[249]. It is a dietary essential for at least the chick, pigeon, and guinea pig. Vitamin B_c may be identical with a spinach concentrate prepared by Williams *et al.* and designated folic acid[250]; it may

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[248] McHenry, E. W., and Gavin, G., *J. Biol. Chem.*, **138**, 471 (1941).

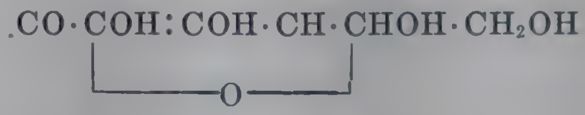
[249] Hogan, A. G., Richardson, L. R., and Johnson, P. E., *J. Biol. Chem.*, **119**, 1 (1937). Hogan and Parrott, E. M., *Proc. Am. Soc. Biol. Chem.*, xlvii (1939). O'Dell, B. L., Hogan, *et al.*, *Id.*, **149**, 323, (1943). Hogan, Richardson, Johnson, and Nisbet, R. N., *J. Nut.*, **20**, 203 (1940). Hogan and Kamm, O., *Science*, **97**, 353 (1943). Pfiffner, J. J., Hogan, *et al.*, *Id.*, p. 404.

[250] Mitchell, H. K., Snell, E. E., and Williams, R. J., *J. Am. Chem. Soc.*, **63**, 2284 (1941).

be identical with the norit eluate factor of Snell and associates, who called it *Lact* *bacillus casei* growth factor[251]; it may be related to the "extrinsic factor" of Min *et al*[252]. A second of these unknowns on which there is an interesting literatu is the "grass-juice factor"[253], richly present in young grass, good silage, and in mil of cows fed on young grass or good silage. There was considerable interest in a "anti-gray hair" vitamin first reported on by Morgan[254] prepared from the "filtrat factors". The "filtrate factor" referred to above is found in water solutions o extracts of liver, yeast, rice-bran, and related substances, after removing thiamine riboflavin, and pyridoxine by shaking with fuller's earth. The "filtrate factor residue contains, among others, pantothenic acid and *p*-aminobenzoic acid, whic some claim to be anti-gray hair factors. It appears, however, that prematur graying of hair may reflect any one of many metabolic disturbances due to the lac of any one of the several nutritional factors. To quote from Adolphus Greely' account of his 1881 Arctic expedition: "When rescued at Cape Sabine my hair wa entirely white, probably due to semi-starvation, and darkened again within a year" The mechanism of graying is a fascinating problem at present under investigation

II. **Ascorbic acid,** vitamin C, anti-scorbutic factor, is water-soluble, but it is not considered to be a member of the B-vitamin or bios family. Like higher animals, some microorganisms synthesize it, others obtain it from the substrate, and still others apparently do not need it at all.

The conspicuous symptom of vitamin C deficiency, in susceptible animals, is scurvy, a disease long known. Its scientific study on the guinea pig as well as on man is associated mostly with Holst and Frölich (1907), with Zilva, who obtained vitamin C in pure form and investigated its properties (1918), and with Szent-Györgyi (1928) and King (1932), who recognized the identity of vitamin C with an oxidation-reduction biocatalyst. Its chemical configuration was determined in 1933 by several groups of workers. Its empirical formula is $C_6H_8O_6$ and its structural formula is variously written as



$$\underbrace{.\mathrm{CO{\cdot}COH{:}COH{\cdot}CH}}_{}{\cdot}\mathrm{CHOH{\cdot}CH_2OH} \quad (\mathrm{CO}\text{—O—}\mathrm{CH})$$

While most animals (primates and guinea pigs excepted) synthesize their own ascorbic acid, its rate of synthesis declines with decline of general vitality due to poor diet and perhaps advancing age, so that old cattle, for example, benefit by ascorbic acid injection. It is a powerful general detoxifying agent, and its administration is helpful during exposure to toxins, disease, and related stresses.

Citrin, vitamin P (P stands for permeability and for paprica from which an extract was made) was reported by Szent-Györgyi[255] as occurring together with vitamin C and having similar functions. It appears to be a component of a hydrogen transport, or of oxidoreduction system[256].

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[251] Snell, E. E., and Peterson, W. H., *et al.*, *J. Bact.*, **39,** 273, 1940; *J. Biol. Chem.*, **141,** 521 (1941).

[252] Minot, G. R., *Lancet*, **1,** 361 (1935). Minot and Murphy, W. P., *J. Am. Med. Assn.*, **87,** 470 (1926). Castle, W. B., *Harvey Lectures*, **30,** 37 (1934–5). Castle and Minot, "Pathological physiology and clinical description of the anemias," New York (Oxford Press), 1936. Bethel, F. H., *et al.*, "Blood: review of recent literature," *Arch. Int. Med.*, **61,** 923 (1938); **63,** 1190 (1939); **64,** 148 (1939).

[253] Hogan, A. G., and Johnson, S. R., *Proc. Soc. Exp. Biol. Med.*, **35,** 217 (1936). Kohler, G. O., Elvehjem, C. A., and Hart, E. B., *J. Nut.*, **14,** 131 (1937); **15,** 445 (1938); **18,** 527 (1939); **20,** 459 (1940).

[254] Morgan, A. F., *Science*, **93,** 261, (1941). Morgan, A. F., and Simms, H. D., "Greying of fur and other disturbances due to a vitamin deficiency," *J. Nut.*, **19,** 233 (1940). "Anti-gray hair vitamin deficiency in the silver fox," *Id.*, **20,** 627 (1940).

[255] Szent-Györgyi, A., *Nature*, **138,** 27 (1936). St. Rusznák and Benkó, A., *Science*, **94,** 25 (1942).

II. Fat-soluble vitamins

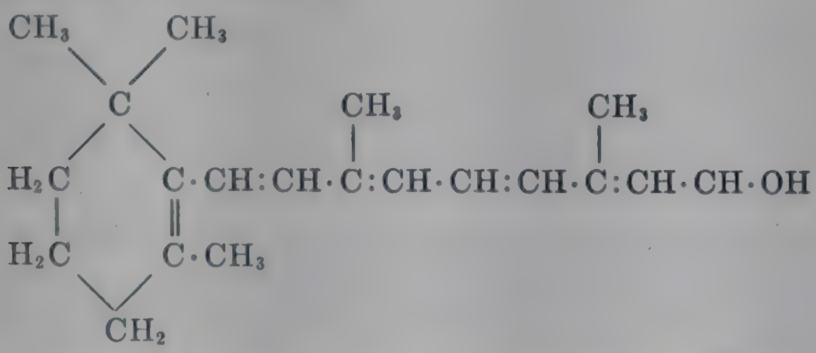
1. *Vitamin A*, antixerophthalmic factor, is a derivative of carotene, $C_{40}H_{56}$ (Willstätter, 1906). The constitution of vitamin A was established by Karrer, Kuhn and Zechmeister in 1931, and Kuhn, Holmes, and others synthesized it in 1937.

The provitamin-A nature of carotene and related substance was demonstrated nutritionally by Steenbock, 1919. The relation between the two is now believed to be:

$$\underset{(C_{40}H_{56})}{1\ \beta\text{-carotene}} + 2H_2O \xrightarrow[\text{in liver}]{\text{carotinase}} \underset{(C_{20}H_{30}O)}{2\ \text{vitamin A}}$$

However, the physiologic efficiency of this conversion is perhaps below 50 per cent, depending on species and other conditions.

The empirical formula of vitamin A is $C_{20}H_{30}O$. The structural formula of vitamin A (half molecule of B-carotene) is:



Karrer received the 1937 Nobel Prize in chemistry for this elucidation.

Vitamin A deficiency leads to many disorders, of which visual and structural disturbances of the eye and inflammation and injury of epithelial tissues are the most conspicuous.

2. *Vitamin D*, antirachitic factor, was recognized to be distinct from vitamin A by Mellanby and by McCollum (1919–22). Of ten-odd D vitamins, only two are practically important, namely D_3 ($C_{27}H_{43}O$), a 7-dehydrocholesterol activated by ultraviolet light, and stored in the liver and skin; and D_2 ($C_{28}H_{43}O$), similarly activated (plant) ergosterol, known as calciferol and viosterol. The activation of ergosterol and cholesterol by ultraviolet light was demonstrated simultaneously by Steenbock and by Hess (1925). This, of course, elucidates the old observation concerning the beneficial effect of light on rickets. Vitamin D is produced not by the organism, but by the action of light on the cholesterol or ergosterol, which are the provitamins, as carotene is of vitamin A.

Windaus isolated, analyzed, and synthesized 7-dehydrocholesterol from cholesterol (1932–5).

The most characteristic syndrome of vitamin D deficiency is softening of the bones, with resulting bow legs, knock knees, pigeon breast, skull-shape abnormalities, and so on. This condition of bone softness in the young is called rickets, and in the old osteomalacia.

3. *Vitamin E*, α-tocopherol, $C_{29}H_{50}O_2$, is mainly known for its effects on reproduction, perhaps by way of the pituitary. Hence the designation for the compounds having this action, as tocopherol, from the Greek for childbearing. The outstanding defi-

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[256] Wanra, C. A., and Webb, L. J., *Science*, **96,** 302 (1942).

ciency symptoms in the male rat is degeneration of the germinal cells of the testes and, therefore, interference with spermatogenesis; in the female rat, interference with placental function, leading to death and resorption of the embryo (Mattill and Conklin, 1920; Evans and Bishop, 1922), hence the designation "resorptive sterility". Many other symptoms have been reported, especially muscular dystrophy (Evans and Burr, 1928; Goettsch and Pappenheimer, 1930) in rats, rabbits and guinea pigs and encephalomalacia and exudative diathesis in chicks. Evans and Burr (1922) recognized the presence of this vitamin (which they called X). Goats do not need vitamin E. Fernholz worked out its chemical configuration (1937), and Karrer and several other groups synthesized it (1938).

4. *Vitamin K*, an antihemorrhagic factor by virtue of the fact that it is the proenzyme of prothrombin which catalyzes the formation of fibrin (in blood clotting) from fibrinogen. Hence, deficiency of vitamin K (often due to obstructive jaundice, biliary fistula, sprue, colitis, liver diseases, etc.) is a frequent cause of intestinal bleeding. The presence of such antihemorrhagic factor was discovered by Dam (1930–4). Doisy *et al.* isolated and synthesized it, as did others (Fieser, Almquist, Ansbacher and Fernholz). There are several vitamin K substances of which K_1 ($C_{31}H_{46}O_2$), a 2-methyl-3-phytyl-1,4-naphthaquinone, and K_2 ($C_{41}H_{56}O_2$), a 2-methyl-3-difornesyl-1,4-naphthaquinone, are the best known.
5. *Fatty acids*[257]. The essential (unsaturated) fatty acids, formerly designated as "vitamin F", function primarily as "building stones", like methionine, previously discussed. Their deficiency produces certain effects similar to vitamin deficiency.

The three major essential fatty acids are:

$CH_3CH_2CH{:}CHCH_2CH{:}CHCH_2CH{:}CH(CH_2)_7COOH$ (linolenic)
$CH_3(CH_2)_4CH{:}CHCH_2CH{:}CH(CH_2)_7COOH$ (linoleic)
$CH_3(CH_2)_4CH{:}CHCH_2CH{:}CHCH_2CH{:}CHCH_2CH{:}CH(CH_2)_3COOH$
(arachidonic)

Exclusion of these fatty acids leads, in the rat, to (1) scaly skin and caudal necrosis; (2) growth retardation; (3) kidney lesions; (4) poor reproductive performance; (5) high water consumption and high R.Q. The kidney lesions are the most reliable deficiency symptoms. Usually the higher the fat consumption the higher the need for the unsaturated acids, as unsaturated fatty acids (linoleic acid) are synthesized to some extent from carbohydrate. Certain eczemas in humans are said to be associated with unsaturated fatty acid deficiency[258].

It was previously noted[133] (Sect. 6.4) that fat has a sparing action on pyridoxine and perhaps on several other vitamins. Corn oil is most effective followed by linseed oil, but not cod liver oil. Corn oil (and presumably others rich in unsaturated acids) is lipotropic, reducing liver fat[257].

IV. Mineral groups in oxidoreductions

The *phosphate group* occupies a central position in catabolic and anabolic processes. Many reactions formerly attributed to or explained by hydrolysis are currently elucidated more rationally (thermodynamically) by phosphorylation. The phosphate group is also a component of many enzymes, as of carboxylase, which is a diphosphothiamine-magnesium protein.

Iron is a component of many hemin catalysts, such as of hemoglobin, cytochrome, catalase.

The *manganese* ion activates many reactions, anabolic and catabolic. The Mg, Mn and Co ions may be interchangeable in some processes.

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[257] Burr, G. O., *Federation Proceedings*, **1**, 224 (1942).
[258] Hansen, A. E., *Am. J. Dis. Child.*, **53**, 933 (1937).

Magnesium is a component of chlorophyll (as iron is of hemoglobin) and of some oxidation catalysts, as of carboxylase (see under phosphate).

Zinc is a constituent of carbonic anhydrase.

Copper catalyzes iron utilization for hemoglobin, and it is a component of many oxidases (polyphenol oxidase, monophenol oxidase, laccase, ascorbic acid oxidase) also of hemocyanin, an analogue of hemoglobin in arthropod and mollusk blood.

Cobalt may serve some similar purpose in ruminants.

Calcium appears to be involved in some oxidase activities.

Vanadium may be involved in phospholipin oxidation.

Nitrogen is, of course, a constituent of thiamine, riboflavin, nicotinamide, pyridoxine, biotin, pantothenic acid, choline, as well as of the hemins (hemoglobin, chlorophyll, cytochromes, etc.).

Sulfur is a constituent of thiamine, biotin, and glutathione*.

In addition to the oxidoreduction processes, many inorganic groups are involved in other types of catalysis, in such physicochemical functions as osmotic pressure, and for structural purposes.

V. General definitions

Oxidation and reduction: loss and gain of electrons or loss and gain of protons. It is generally accepted that biologic oxidoreductions are stepwise processes; by enzymatic electron-transfer systems, the *ultimate* electron (and hydrogen) acceptor in *aerobic* oxidation is atmospheric oxygen, forming H_2O; in anaerobic oxidation (fermentation, glycolysis, internal oxidoreduction) the electron acceptor is formed by the electron donor. The metabolites undergoing oxidation are the electron (and hydrogen) donors. The conspicuous catalysts in anaerobic oxidation are pyridine and thiazole enzymes; in aerobic oxidation, also alloxazine and hemin catalysts.

Oxygen debt: anaerobic oxidation in higher animals during intense muscular work when the oxygen supply is inadequate, and intermediate metabolic products accumulate. Recovery occurs when the oxygen supply becomes adequate, and the intermediate products are oxidized.

Oxidation-reduction potential: the electric potential of an element in contact with a solution of its ions at unit activity, referred to that of hydrogen (under standard conditions) as zero.

Oxidation-reduction indicator: a substance existing in oxidized and reduced form and changing color with change in the O–R potential.

Phosphorylation: combination of metabolite with phosphate, under the influence of certain catalysts (see glycolysis), especially adenyl pyrophosphate, which is the phosphate "carrier". Adenyl pyrophosphate is composed of one adenylic acid, and two phosphate groups which are "donated" to the metabolite, thus:

$$\text{glucose} + \text{adenyl pyrophosphate} \rightarrow \text{hexose diphosphate} + \text{adenylic acid.}$$

Adenylic acid is involved in alcohol formation from hexose diphosphate, thus:

$$\text{phosphoric ester} + \text{adenylic acid} \rightarrow \text{adenyl pyrophosphate} + \text{alcohol} + CO_2$$

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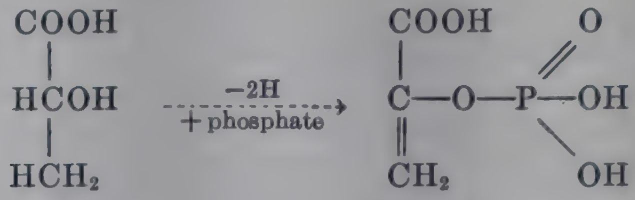
[*] Glutathione is a tripeptide consisting of glutamic acid, glycine, and cystein ($CH_2SH \cdot CHNH_2 \cdot COOH$). Sulfhydryl is the SH in the cysteinyl group. There is an immense literature on the function of glutathione, which may be summarized, from the oxidoreduction viewpoint, by the equation:

$$\underset{\substack{\textit{(glutathione sulfhydryl,}\\ \textit{reduced)}}}{2GSH + B} \rightleftharpoons \underset{\substack{\textit{(glutathione disulfide,}\\ \textit{oxidized)}}}{GSSG + BH_2}$$

Two molecules of —SH (written GSH) are oxidized to one of —S—S— (written GSSG). This is reversible: glutathione reduces ascorbic acid (after oxidation by ascorbic oxidase), thus serving as an electron carrier.

Most electron donors (metabolities) must be phosphorylated as the preliminar step; for phosphorylation and oxidation are indeed *coupled* reactions. A possibl example of phosphorylation (Kalckar), forming phosphate-ester bonds, the sourc of anaerobic energy (Lipmann):



lactic acid *phosphopyruvic acid*

Glycolysis: conversion of carbohydrate to lactate by a series of catalysts, as phosphorylase, phosphatase, aldalase, enolase, dehydrogenase, adenyl pyrophosphate, Mg^{++}, Mn^{++}, and others. This, as other intermediary processes, may be blocked (Lundsgaard, Krebs) in any of its stages by various "poisons", such as iodoacetate, fluoride, heavy metal, and by certain enzymes as by amylase [Case and McCullagh, *Biochem. J.*, **22,** 1060 (1928); Ronzoni, *Proc. Soc. Exp. Biol. Med.*, **25,** 178 (1928–8)].

Glycogenolysis: conversion of glycogen to glucose; *glycogenesis:* conversion of glucose to glycogen.

Gluconeogenesis: formation of glucose from protein or fat.

Oxidase: enzyme which "activates" oxygen (Warburg).

Dehydrogenase: enzyme which "activates" hydrogen (Wieland-Thunberg).

Carrier: "accepts" hydrogen and is thereby reduced, and then "donates" it to another acceptor and is thereby oxidized. "Carriers" are thus reversibly reduced and oxidized.

Dehydrogenation: is the catalytic transfer of hydrogen (by a "carrier" enzyme).

Example: Methylene blue is reversibly reduced (to colorless) by hydrogen and oxidized (to blue) by oxygen, thus transferring H from donator (metabolite) to oxygen (Thunberg).

Example: $CH_3 \cdot CHOH \cdot COOH \xrightarrow[\text{dehydrogenase}]{\text{lactic}} CH_3CHO \cdot COOH + 2H$

Proenzyme, prosthetic group: a precursor of an enzyme, formed near the place of the enzyme action; the active part of an enzyme. Thiamine may be considered as proenzyme or prosthetic group of cocarboxylase (diphosphothiamin protein); nicotinic acid of coenzyme I (diphosphopyridine nucleotide or simply pyridine protein); riboflavin of yellow enzyme (flavin-adenine-nucleotide); carotene of vitamin A; vitamin A of visual protein; vitamin K of prothrombin; cholesterol and ergosterol of vitamin D; iron of iron protoporphyrin or hemin, as of hemoglobin and cytochrome; copper of hemocyanin and of certain oxidases. Similarly iodine may be considered as a prosthetic group of thyroxine, and thyroxine a prosthetic group of thyroglobulin.

Metabolism: the sum total of the chemical changes in the body, including the building up (anabolic, assimilation) and the breaking down (catabolism, dissimilation) processes.

Vitamin applications (Ch. 20): (1) understanding biologic oxidoreduction mechanisms; (2) effect on more complete utilization of feed or food for productive purposes; (3) "detoxifying effects" of some of the water-soluble vitamins under certain conditions on, for example, gold, lead, sulfa drugs, alcohol, thyroxine, some bacterial toxins, pyruvic, lactic, and acetoacetic acids, histamine (as in hay fever). It is probable that some cortical-adrenal hormones have similar effects. Unlike thyroxine, excess intake of the water-soluble oxidation-reduction vitamins is apparently harmless[259], as it is easily excreted through the kidney and sweat glands. Less is known about the effects of excessive and vitamins D and A and some other fat-soluble vitamins.

Quantitative estimation of the need for each of the several vitamins and related factors is confused by their sparing, synergistic, supplementary and antagonistic interrelations. For instance[260], vitamin E (tocopherols and also tocoquinones) retard oxidation of vitamin A and carotene; hence the amount of vitamin A or carotene needed is reduced by the presence of vitamin E and conversely, deficiency of vitamin E may result in deficiency of vitamin A. Vitamin E is thus said to have a "covitamin A" activity[260]. Then, too, some nutrients may actually replace others, serving the same nutritional purpose, acting as "isotels"[261] (iso, the same; telos, purpose). For instance, nicotinamide and nicotinic acid are "isotelic"; they serve the same purpose in nutrition. Pantothenic acid and beta-alanine are "isotelic" in yeast nutrition. Choline and methionine may replace each other in that both furnish methyl groups, and these are also interrelated with pyridoxine, inositol, essential fatty acids and essential amino acids in their lipotropic action[262]. Thiamine appears to be essential for the production of ascorbic acid in dogs[263] and vitamin A is necessary for the production of ascorbic acid in cattle[127]. Avidin, biotin, and the bacteriostatic substance "lysozone" of Fleming and Allison[264] appear to be interrelated[265]. (Biotin may be the "active" principle of lysozone and the avidin acts as "binder" in the "enzyme" system.)

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[259] Molitor, H., *Federation Proceedings*, **1**, 309 (1942).

[260] Hickman, K. C. D., *et al.*, *J. Biol. Chem.*, **152**, 303, 313, 321 (1944). Davies, A. W., and Moore, T., *Nature*, **147**, 794 (1941).

[261] Williams, R. J., *Science*, **98**, 386 (1943).

[262] Beveridge, J. M. R., *Id.*, **99**, 539 (1944); *J. Biol. Chem.*, **154**, 9 (1944).

[263] Govier, W. M., and Greig, M. E., *Science*, **98**, 216 (1943).

[264] Thompson, R., *Arch. Path.*, **30**, 1096 (1940).

[265] Meyer, K., and Laurence, W. L., *Science*, **99**, 391 (1944).

Chapter 7

Metabolic Catalysts in the Efficiency Complex: Hormones

> It is the avowed purpose of scientific thought to reduce the number of mysteries, and its success has been marvelous. *J. H. Robinson.*

7.1: Orientation. As previously explained (Ch. 6) there is no sharp dividing line between vitamins, *i.e.*, *exogenous catalysts* taken with the food, and hormones or enzymes, *i.e. endogenous catalysts* produced within the body. Thus, ascorbic acid is an exogenous catalyst—a vitamin—in man, monkey, and guinea pig, and an endogenous catalyst in other species examined, including the chick embryo (thus excluding possible vitamin C production by intestinal flora). Likewise, the rat is independent of dietary biotin, folic acid, nicotinic acid, and vitamin K which some other species must obtain from food[1].

Clearly, only such substances can be vitamins as are not digested during their passage through the digestive tract and are composed of sufficiently small molecules to be readily absorbed from the digestive tract into the blood. The hormones, on the other hand, need not be so stable nor the molecules so small. The body may have evolved mechanisms for producing internally such catalysts as could not pass through the digestive tract, such as insulin, or which could not reliably be obtained from food, as can ascorbic acid in temperate climate (Ch. 6). The peculiarity of some hormones of being destroyed in the digestive tract was not fully appreciated in early investigations. Thus about 1914 Robertson, Professor of Biochemistry at the University of California, formulated an apparently correct theory of anterior-pituitary hormone function in growth[2], but he attempted to prove it by feeding pituitary. Evans, Professor of Anatomy at the same institution, however, injected the pituitary substance, with the well-known results to be discussed presently.

The endocrine glands are very small bodies (for detailed weights see Ch. 17). Remembering that 1 ounce is about 28.3 grams or 1 gram is 1/28.3 ounce, the pituitary in

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[1] "Synthetic diets" which support growth and reproduction in the rat do not permit survival in the monkey or guinea pig even if vitamin C and the other available vitamins are added. Waisman, H. A., Rasmussen, A. F., Jr., Elvehjem, C. A., and Clark, P. J., *J. Nut.*, **26**, 205 (1943).

[2] Robertson, T. B., "Principles of biochemistry," 1919, and "Biochemical basis of growth and senescence", Philadelphia, 1922. See, however, Robertson, *J. Biol. Chem.*, **24**, 385 (1916).

-kg animals (weight of an average man or sheep) weighs only about 0.6 g, which is bout 0.0008 per cent of the total body weight. Likewise in mature 70-kg animals the hyroids, one on each side of the trachea, weigh about 6.5 g, which is about 0.009 per ent of the body weight; the parathyroids, usually four glands imbedded in the thyroids, eigh together in mature 70-kg animals about 0.2 g; the adrenals or suprarenals, situated bove the kidneys, weigh about 8 g; the gonads, ovaries and testes weigh in mature an about 10 and 25 g, respectively.

Most glands produce more than one hormone and some have more than one anatomic part. Thus the adrenals or suprarenals have a medullary (central) part producing adrenaline and a cortical (shell) part producing adrenocortical hormones. The pituitary, or hypophysis, has a posterior lobe producing pituitrin (pitressin and pitossin or oxytocin) and an anterior lobe producing especially gland activators or, as they are called, trophic or tropic[3] hormones, wherewith it controls many other endocrine glands, especially the adrenals, thyroids, and gonads. Thus the anterior pituitary controls the gonads by gonadotropic hormones, or gonadotropins. The gonadotropins stimulate the gonads (ovaries and testes) to produce sex hormones (estrogen, progesterone, androgen). The familiar sex processes are thus controlled directly by the sex hormones and indirectly by the anterior-pituitary gonadotropins.

Hormones are said to differ from vitamins and enzymes by their endocrine-gland origin. But hormones are not always produced by specialized endocrine glands as usually understood. Thus following the early period of gestation, the sex hormone progesterone is produced mostly by the placenta[4], which is not thought of as an endocrine, rather than by the corpus luteum, the ovarian progesterone-producing endocrine gland. Gonadotropins, normally produced by the pituitary gland, are produced in great quantities by the placenta (chorionic and equine gonadotropins) during gestation[5]. Indeed, the Ascheim-Zondek pregnancy test[6] is based on the excretion of chorionic gonadotropins in the urine; and these placental or chorionic gonadotropins, like the pituitary gonadotropins, function therapeutically in hypogenitalism, cryptorchidism, and in growth acceleration[7]. It appears that during gestation many pituitary functions are taken over by the placenta[8]. Moreover, nerve endings, not thought of as endocrine glands, liberate such hormones as acetylcholine[9] and sympathin, and embryonic tissues produce various categories of hormones (organizers, evocators, etc.).

Some hormones, such as thyroxine may be taken by mouth. Some steride (sex) hormones may even be absorbed through skin[10], especially mucous membrane. Most hormones are, however, proteins of high molecular weight which cannot pass into the body without digestion.

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[3] Corner, G. W., *Endocrinology*, **33**, 405 (1943). Corner prefers "trophic".

[4] Venning, G. E., and Browne, S. L., *Endocrinology*, **21**, 722 (1937). Hart, G. H., and Cole, H. H., *Am. J. Physiol.*, **109**, 320 (1934).

[5] Collip, J. B., *International Clinics*, **4**, 51 (1932). Gurin, S., *et al.*, *Science*, **92**, 456 (1940).

[6] Salmon, U. J., *et al.*, *J. Clin. Endocr.*, **2**, 167 (1942). Burdick, H. P. *Id.*, **33**, 1 (1943).

[7] Finkler, R. S., *et al.*, *Id.*, p. 603 (1943).

[8] Hartman, C. G., *Proc. Soc. Exp. Biol. Med.*, **48**, 221 (1941). Newton, W. H., *Physiol. Rev.*, **18**, 419 (1938).

[9] Nachmansohn, D., *et al.*, *J. Neurophysiol.*, **4**, 348 (1941); **5**, 499 (1942); **6**, 383, 397 (1943).

[10] Moore, C. R., *et al.*, *J. Am. Med. Assn.*, **111**, 11 (1938).

Hormones are also more complex than vitamins in that while many vitamin reactions may occur in test tubes in the absence of living tissue, hormone reactions apparently cannot be dissociated from living cells. This explains the relative abundance of information on the anatomic and physiologic aspects of endocrinology and scarcity of information on the biochemical mechanisms of hormone action. Biochemical progress has thus far been confined to the isolation, identification, estimation, and synthesis of hormones; little is known about the intimate biochemical hormone mechanisms.

The catalytic functions of hormones appear to be similar to those of vitamins. Thus carbohydrate metabolism involves the catalytic participation of thiamine, riboflavin, and nicotinic acid (Ch. 6), and it also involves insulin, anterior pituitary factors, corticosterone, and adrenaline. In some cases there is a known or a guessed functional interrelation between vitamins, hormones, and enzymes, as for example, between adrenaline, glutathione, ascorbic acid, and cytochrome c.

The biologic effectiveness is probably of the same order, 1 to millions or even to billions[11], for vitamins and hormones.

There is another interesting relation between vitamins, hormones, and some other substances illustrated in Fig. 7.1. The sex hormones, the D vitamins, adrenal cortex hormones, bile acids, saponins, and some carcinogens are phenanthrene compounds; they contain the cyclopentano-phenanthrene nucleus (cholesterol nucleus). Many differences, such as those between male and female sex hormones, are very slight, differing only in saturation, in a side chain, or even only in the position of a double bond.

In chemical structure vitamin D is similar to sex hormone, and in function it is similar in some respects to parathyroid hormone (regulating calcium metabolism). However, sex hormones also participate in calcium and other forms of metabolism[12].

An inferred analogy between vitamins and hormones relates to what might be called *anti*-vitamin and *anti*-hormone effects of some substances. It is believed that the sulfa drugs (sulfanilamide, sulfapyridine, sulfathiazole, sulfaguanidine, sulfadiazine, sulfamerazine, sulfasuxidine, succinyl-sulfathiazole, etc.) owe their anti-bacterial potency to their structural similarity to an essential bacterial growth factor, as to *p*-aminobenzoic acid[13] (Fig. 6.2), and thus compete with *p*-aminobenzoic acid for an enzymatic system involved in bacterial growth. There is similar antagonism between sulfapyridine, or

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[11] Kögl, F., and Tonnis, B., *Z. Physiol. Chem.*, **242,** 43 (1936) (biotin, 1 to 400 billion). Adrenaline is effective in concentrations of 1 to 400 million. The whole human body contains less than 20 mg of thyroxine.

[12] Gardner, W. U., and Pfeiffer, C. A., *Physiol. Rev.*, **23,** 139 (1943).

[13] Woods, D. D., *Brit. J. Exp. Path.*, **21,** 74, (1940). Burton, H., *et al.*, *Path. Bact.* **54,** 407 (1942).

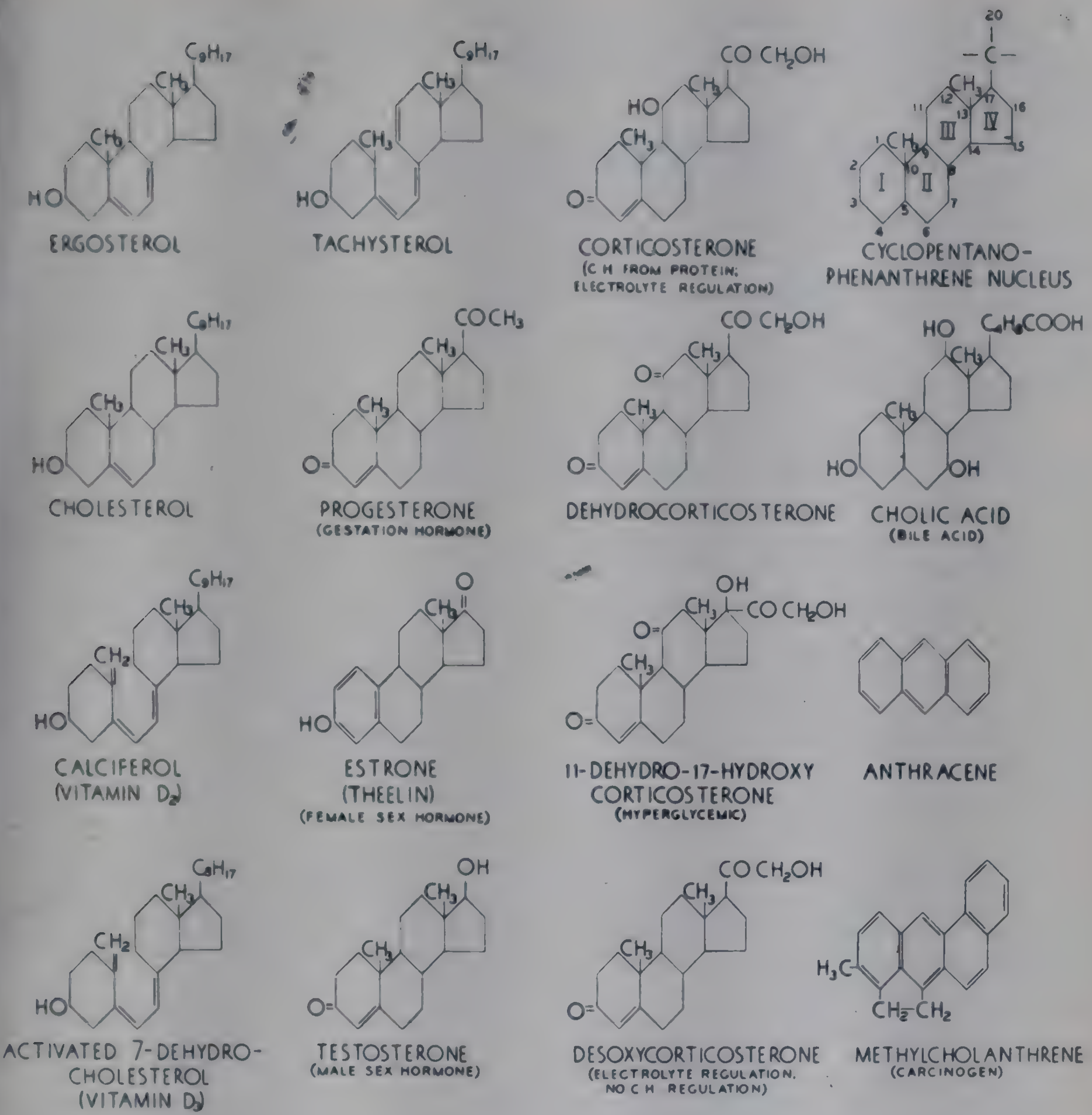

Fig. 7.1—Configurational relationship between the formulas of ergosterol (plant sterol), cholesterol (animal sterol), calciferol (vitamin D from ergosterol), activated 7-dehydrocholesterol (vitamin D from cholesterol), tachysterol (from ergosterol, an intermediate product between ergosterol and calciferol often used in parathyroid deficiency), progesterone, typical female sex hormones (estrone and progesterone), typical male sex hormone (testosterone), adrenal cortical hormones (corticosterone derivatives), bile acid (cholic acid), a typical carcinogen (methylcholanthrene).

sulfamerazine, and nicotinic acid[14], both containing a pyridine group. The sulfa drugs may thus be viewed as antivitamin. There may be similar drugs inactivating other vitamins, such as pyrithiamine inactivating thiamine[15].

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[14] West, R., *Proc. Soc. Exp. Biol. Med.*, **46**, 679 (1942). Light, R. F., *et al.*, *J. Nut.*, **24**, 427 (1942). Teply, L. J., Axelrod, A. E., and Elvehjem, C., *J. Pharm.*, **77**, 207 (1943).

[15] Wooley, O. W., *J. Biol. Chem.*, **149**, 285 (1943); *Proc. Soc. Exp. Biol. Med.*, **52**, 106 (1943). Wyss, O., *et al.*, *Id.*, 155. Wooley and White, A.G.C., *J. Exp. Med.*, **78**, 489 (1943).

It may be cogent to note in this connection that when 2 to 5 per cent sulfur is added to a chicken ration, the vitamin D in the cod liver oil therein is no longer effective[16].

There are similar anti-thyroid drugs[17], thiourea and aniline derivatives, especially 2-thiouracil (NHCSNHCOCHCH), 2-thiobarbituric acid, and so on; *p*-aminobenzoic acid ($NH_2C_6H_4COOH$), sulfaguanidine, sulfapyridine, sulfathiazole, etc., which inhibit thyroxine production, perhaps because of their structural similarity to the thyroxine precursor tyrosine and because they compete with it for the enzyme system involved in the production of thyroxine from diiodotyrosine.

These facts and theories on the similarity of the sulfa anti-vitamin drugs and anti-thyroid drugs lead to the thought that the hormone-like carcinogens, exogenous and endogenous (as methylcholanthrene, Fig. 7.1) may, perhaps, likewise interfere with the normal action of some cellular enzyme system[18] and thus change a normal cell to a cancer cell. Increasing age is often associated with metabolic abnormalities, especially of the sex and adrenal-steride hormones, as judged by increasing age incidence in their dysfunction. This may, perhaps, explain the mechanism whereby castration prevents and alleviates prostate cancer[19] and, perhaps, cancer of other genital tissues. Similarly, ovariectomy reduces cancer incidence[20], and estrogen injection increases it.[20] A spectacular associative feature of prostatic carcinoma is a high concentration of the enzyme acid phosphatase in the blood[18]; this declines sharply on castration. Castration perhaps eliminates the production of some atypical sterides associated with aging, which, analogous to the sulfa drugs in relation to *p*-aminobenzoic acid or nicotinic acid, interfere with normal enzyme processes. A similar situation may hold for adrenalectomy, as the adrenal cortex produces many sex-like steroids. The apparent necessity of pituitary presence for genital-cancer induction substantiates this suggestion of the hormone-like nature of some carcinogens, and of their probable competitive interference with normal function.

The carcinogenic effect on liver of feeding the azo dye "butter yellow"[21] to rats kept on a riboflavin-low diet was explained by a similar mechanism[22]. A metabolic product of this dye, such as *p*-aminophenol, probably interferes with normal enzymatic activity, which in turn may be compensated by adding more riboflavin, preferably in the form of yeast and liver.

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[16] Holmes, C. E., *Poultry Sci.*, **17,** 136 (1938).

[17] Mackenzie, J. B., and C. G., and McCollum, E. V., *Science*, **94,** 518 (1941); *Fed. Proc.*, **1,** 122 (1942) (sulfaguanidine); *Endocrinology*, **32,** 185 (1943) (sulfanilamides and thioureas). Richter, C. P., and Clisby, K. H., *Proc. Soc. Exp. Biol. Med.*, **48,** 684 (1941) (phenylthiourea), and *Arch. Path.*, **33,** 46 (1942). Kennedy, T. H., *Nature*, **150,** 233 (1942) (allylthiourea). Carter, G. S., *et al.*, *Nature*, **151,** 728 (1943) (paraxanthine). Astwood, E. B., *J. Pharm. Exp. Ther.*, **78,** 79 (1942) (106 drugs); *J.A.M.A.*, **122,** 78 (1943); *Endocrinology*, **32,** 210, 509 (1943). Williams, R. H., and Bissell, G. W., *New Eng. J. Med.*, **229,** 97 (1943); *Science*, **98,** 156 (1943). Gordon, A. S., *et al.*, *Nature*, **152,** 504 (1943). Martin, G. J., *Arch. Bioc.*, **3,** 61 (1943–44).

[18] For tumor enzymology, see Greenstein, J. P., *J. Nat. Cancer Inst.*, **3,** 419 (1943).

[19] Huggins, C., and Hodge, C., *Cancer Res.*, **1,** 293 (1941); *Arch. Surg.*, **43,** 209 (1941). Huggins, C., *Science*, **97,** 504, 541 (1943); *N. Y. Acad. Med.*, **19,** 195 (1943). Estrogen administration is also used instead of castration in prostate hypertrophy. Kahle, P. J., *et al.*, *J. Urol.*, **48,** 83 (1942), Lane, T. J. D., *Lancet*, **1,** 166 (1943). Neuswanger, C. H., and Vermooten, V., *N. Eng. J. Med.*, **227,** 626 (1942). For contrary results, see Kretschmer, H. L., *J.A.M.A.*, **123,** 755 (1943).

[20] Loeb, J., *J.A.M.A.*, **104,** 1597 (1935); *Am. J. Cancer*, **30,** 47 (1937). Robson, J. M., and Bonser, G. M., *Nature*, **142,** 836 (1938). Allen, E., *J.A.M.A.*, **114,** 210 (1940). Geschichter, C. F., *et al.*, *Arch. Path.*, **33,** 334 (1942); *J.A.M.A.*, **119,** 885 (1942) and references on the following pages.

[21] Sasaki, T., and Yoshida, T., *Virch. Arch. Path. Anat.*, **295,** 175 (1935).

A curious aspect relating to the yeast-liver *anti*-carcinogenic action of the dye "butter yellow" is that the vitamin biotin (anti-avidin factor) neutralizes the protective effect of the yeast or liver; biotin is *pro*carcinogenic under the given conditions[23]. We thus have a fascinatingly complex problem involving interrelations between carcinogens, hormones, vitamins, and enzymes bearing on one of the most puzzling medical and biological problems—cancer.

A spectacular type of cancer is one produced in the breast of some strains of mice that received during suckling a "mammary tumor inciter"[24], apparently nucleo-protein in nature. This inciter apparently becomes active only in late life under the influence of estrogen or carcinogenic provocators[25]. Similar tumor inciters may, of course, be absorbed during uterine life. An enzyme-virus theory of carcinogenesis has been suggested[26].

Cancer incidence is a function of (1) tissue susceptibility, (2) level or action frequency of causative factor, and (3) time of influence.

The time element[27] is, of course, an important factor in cancer induction. The longer one lives, the greater the provocations; the longer the period of exposure, the greater the probability of a mishap, especially since increasing age is associated with increasing dysfunction, increasing number and amount of atypical metabolic products, especially of sex-hormone origin, and cumulative excitation and trauma by the cyclically acting sex hormones. It has, indeed, been demonstrated[28] that heavy repetitive estrogen injection induces genital cancer, especially breast cancer.

While hormones are named by their most spectacular effects, as "sex hormones", all hormones are, in fact, *general metabolic* hormones; they are all involved in the transformation of energy-matter. Thus the thyroid is involved not merely in energy metabolism but in virtually every process in the body, including mineral metabolism, sex activity, growth and development, and so on. The same is true for every hormone; they are all interrelated and exert wide-spread effects. However, the precise influence of a given endocrine depends on the age of the organism and on the scope of interrelation.

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[22] Rhoads, C. P., *et al.*, *Science*, **93**, 308 (1941); *Cancer Res.*, **1**, 3 (1941); *N. Y.Acad. Med.*, **18**, 53 (1942).

[23] du Vigneaud, V., Rhoads, C. P., *et al.*, *Science*, **95**, 174 (1942).

[24] Bittner, J., *J. Cancer Res.*, **2**, 711 (1942); *Science*, **95**, 462 (1942).

[25] Gardner, W. U., *Cancer Res.*, **1**, 109 (1941). Rous, Peyton, *J.A.M.A.*, **122**, 573 (1943). For chemical cancinogens see: Fieser, L. F., "Products related to phenanthrene," Reinhold, 1936; "Cause and growth of cancer", Univ. Pennsylvania Press, 1941. Dodds, E. C., *Nature*, **148**, 142 (1941).

[26] Potter, V. R., *Cancer Res.*, **3**, 358 (1943). White, P. R., *Science*, **98**, Supplement, p. 10 (1943); especially Smith, J. L., "Growth", Edinburgh, 1932.

[27] *Cf.*, Cramer, W., *J.A.M.A.*, **119**, 309 (1942); *Yale J. Biol.*, **14**, 121 (1942). Bittner, J. J., *et al.*, *Science*, **99**, 83 (1944).

[28] Gardner, W. U., *et al.*, *Proc. Soc. Exp. Biol. Med.*, **33**, 148 (1935). Zuckerman, S., Lacquer, E., *et al.*, *Lancet*, **2**, 1259, 1433 (1936). For review of Edgar Allen's book, see Allen, *J.A.M.A.*, **114**, 2107 (1940); *Endocrinology*, **30**, 942 (1942). Lacassagne, A., *Am. J. Cancer*, **37**, 414 (1939). Loeb, J.,[20] and *J. Nat. Cancer Inst.*, **1**, 169 (1940). Auchincloss, H., and Haagensen, C. D., *J.A.M.A.*, 114, 151 (1940); Geschichter,[20] (1942), and many others.

Thus the early chick embryo does well enough without endocrines[29], but at later ages the endocrines and their hormones become crucial. Likewise, the effect of the pituitary sex hormones (gonadotropins) on sex activity varies with age[30]. Administration of some hormones, including anterior pituitary, thyroid and sex hormones, may accelerate growth and senescence at the same time[31].

As regards the scope of interrelation, some important endocrines, such as the gonads, may be removed with much less effect on general metabolism than others, such as thyroid, adrenal, pituitary. The extirpation of the pituitary is particularly serious, throwing out of gear practically all other endocrines and consequently all productive processes.

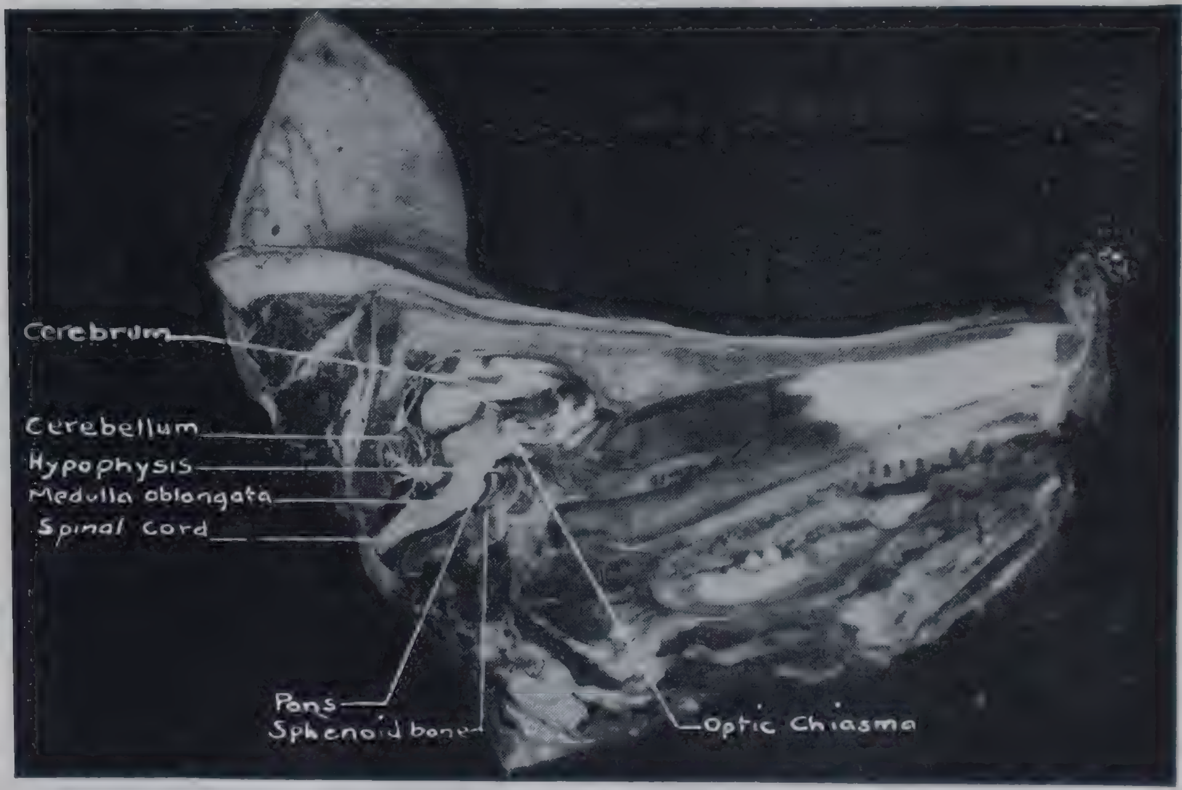

Fig. 7.2a—The pituitary or hypophysis, its position and relative size in 175 to 250 pound hogs (for pituitary weights, see Ch. 17). Figs. 7.2a-d courtesy H. D. Elijah and C. W. Turner, Univ. Missouri Agr. Exp. Sta. Res. Bull. 357, 1942.

The pituitary exerts the widest influence by way of its tropic hormones[32] (Figs. 7.2 and 7.3). To illustrate, sex activity is controlled by the anterior pituitary (A.P.) gland. The A.P. elaborates, among others, two gonadotropic hormones: (1) F.S.H. (follicle-stimulating hormone), involved in the maturation of egg or sperm, graafian follicles, and secretion of estrogens; (2) L.H. or I.C.S.H. (luteinizing or interstitial cell-stimulating hormone, the two appear

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[29] Fugo, N. W., *J. Exp. Zool.*, **85**, 271 (1940).

[30] Selye, H., and Albert, S., *Proc. Soc. Exp. Biol. Med.*, **49**, 361; **50**, 159 (1942).

[31] Silberberg, M. and R., *Arch. Path.*, **36**, 512 (1943).

[32] Van Dyke, H. B., "The physiology and pharmacology of the pituitary body," University of Chicago Press, 1936-1943. Smith, P. E., *J.A.M.A.*, **115**, 1991 (1940). Collip, J. B., *Id.*, **115**, 2073 (1940). Engle, E. T., and Levin, L., *Id.*, **116**, 47 (1941), and many others

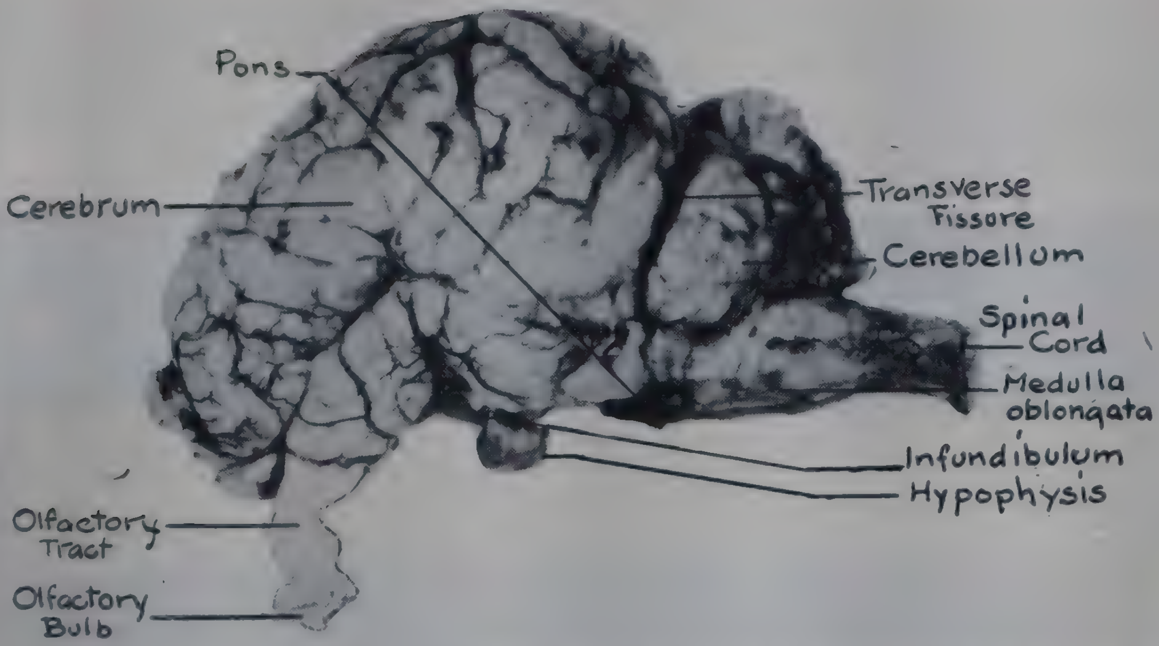

Fig. 7.2b—The pituitary or hypophysis, its position and relative size in 175 to 250 pound hogs (for pituitary weights, see Ch. 17).

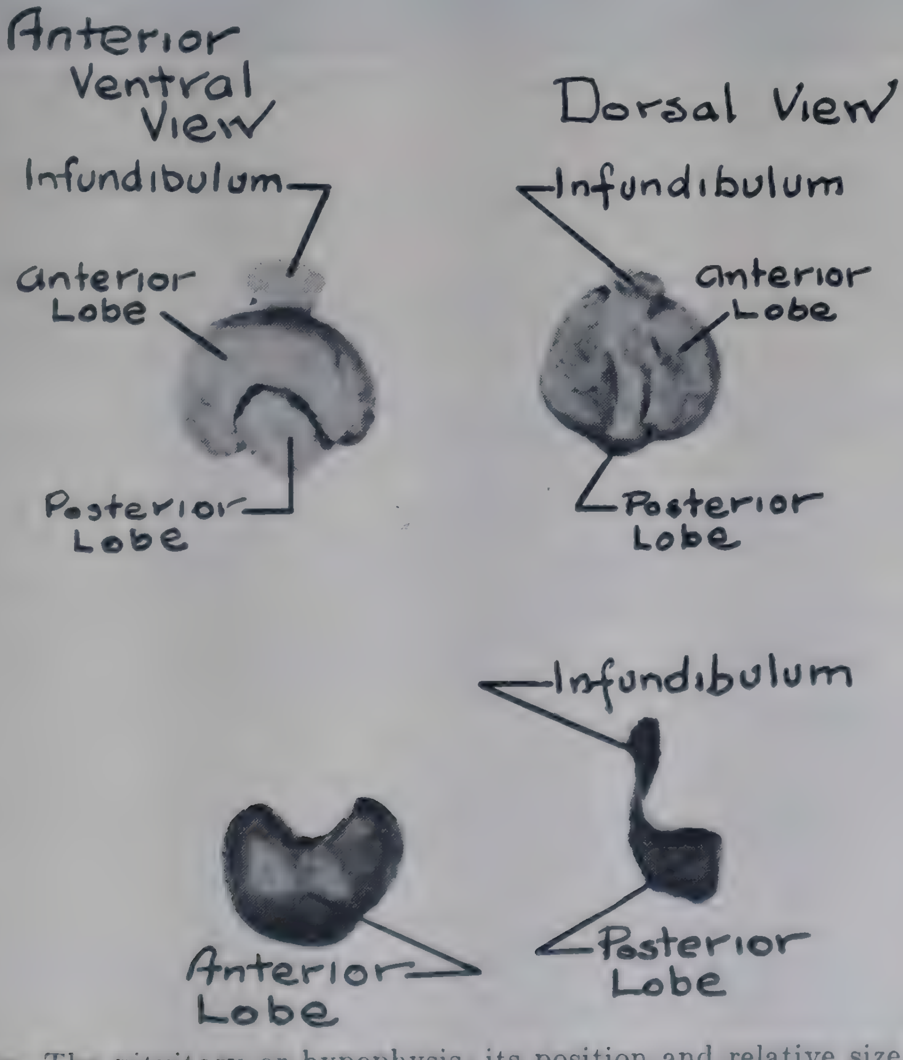

Fig. 7.2c—The pituitary or hypophysis, its position and relative size in 175 to 250 pound hogs (for pituitary weights, see Ch. 17).

to be identical)[33] involved in secretion of progesterone and inhibition of estrogen secretion, and in males in stimulation of the testicular interstitial cells an androgen production. Lack of pituitary sex hormones arrest sexual development, resulting in such abnormalities as the Fröhlich syndrome.

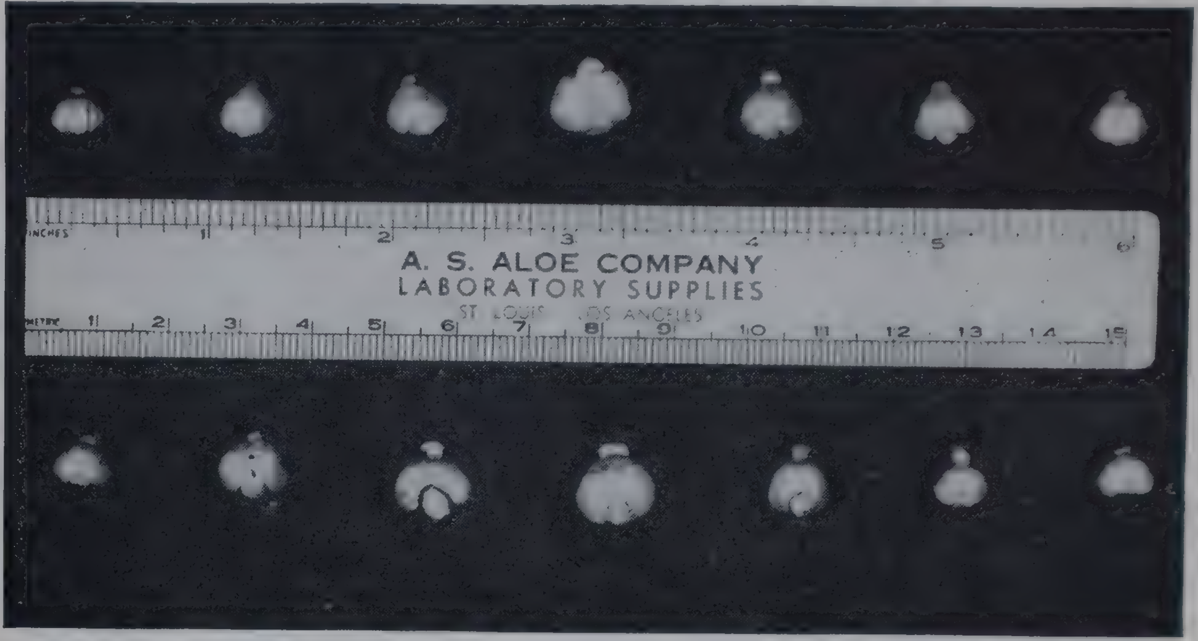

Fig. 7.2d—The pituitary or hypophysis, its position and relative size in 175 to 250 pound hogs (for pituitary weights, see Ch. 17).

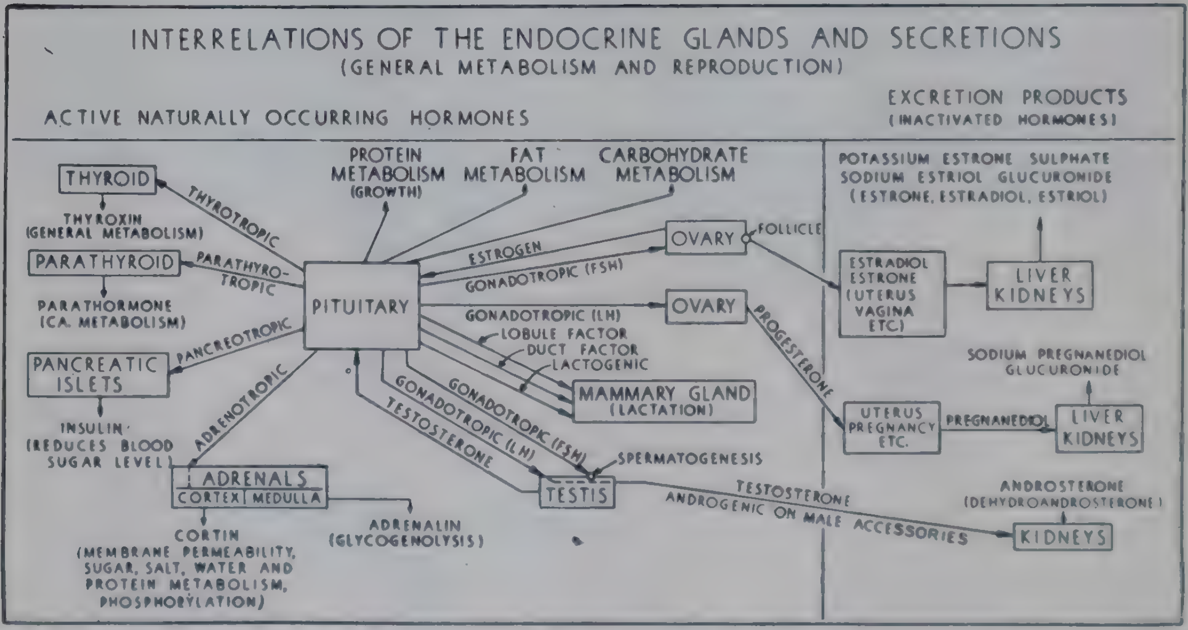
INTERRELATIONS OF THE ENDOCRINE GLANDS AND SECRETIONS
(GENERAL METABOLISM AND REPRODUCTION)
ACTIVE NATURALLY OCCURRING HORMONES
EXCRETION PRODUCTS (INACTIVATED HORMONES)
PROTEIN METABOLISM (GROWTH)
FAT METABOLISM
CARBOHYDRATE METABOLISM
THYROID
THYROTROPIC
THYROXIN (GENERAL METABOLISM)
PARATHYROID
PARATHYROTROPIC
PARATHORMONE (CA. METABOLISM)
PANCREATIC ISLETS
PANCREOTROPIC
INSULIN (REDUCES BLOOD SUGAR LEVEL)
ADRENOTROPIC
ADRENALS
CORTEX
MEDULLA
CORTIN (MEMBRANE PERMEABILITY, SUGAR, SALT, WATER AND PROTEIN METABOLISM, PHOSPHORYLATION)
ADRENALIN (GLYCOGENOLYSIS)
PITUITARY
ESTROGEN
GONADOTROPIC (FSH)
OVARY
FOLLICLE
GONADOTROPIC (LH)
OVARY
PROGESTERONE
LOBULE FACTOR
DUCT FACTOR
LACTOGENIC
MAMMARY GLAND (LACTATION)
GONADOTROPIC (FSH)
GONADOTROPIC (LH)
TESTOSTERONE
SPERMATOGENESIS
TESTIS
TESTOSTERONE
ANDROGENIC ON MALE ACCESSORIES
POTASSIUM ESTRONE SULPHATE
SODIUM ESTRIOL GLUCURONIDE
(ESTRONE, ESTRADIOL, ESTRIOL)
ESTRADIOL ESTRONE (UTERUS VAGINA ETC.)
LIVER KIDNEYS
SODIUM PREGNANEDIOL GLUCURONIDE
UTERUS PREGNANCY ETC.
PREGNANEDIOL
LIVER KIDNEYS
ANDROSTERONE (DEHYDROANDROSTERONE)
KIDNEYS

Fig. 7.3a—The position of the pituitary in relation to the hormonal configuration. Courtesy Dennis T. Mayer, Missouri Agr. Exp. Sta.

Now, just as the pituitary controls gonadal activity by its gonadotropic hormones, so it controls thyroid activity by its thyrotropic hormone, adrenal activity by adrenotropic or corticotropic hormone, and so on. Among other pituitary tropic hormones believed to exist are parathyrotropic, pancreatropic stimulates insulin production), glycotropic (anti-insulin), diabetogenic (in-reases sugar production), ketogenic (accelerates fat metabolism and ketone-ody production), lactogenic (prolactin), mamogenic (Fig. 7.3b) somatropic growth), and so on. The presence of some of these pituitary tropic hormones, such as the pancreatropic, is still under investigation.

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[33] Evans, H. M., *et al.*, *Endocrinology*, **27**, 803 (1940); *J. Am. Chem. Soc.*, **64**, 367 (1942 Van Dyke, H. B., *et al.*, *Id.*, **30**, 650 (1942) (L. H. is identical with I.C.S.H.).

The anterior pituitary is the central mediating station through which various environmental factors, such as season (Ch. 8), food supply (Chs. 6 and 20), and psychic stimuli (Ch. 10), control the sex cycle and other neuro-endocrine activities.

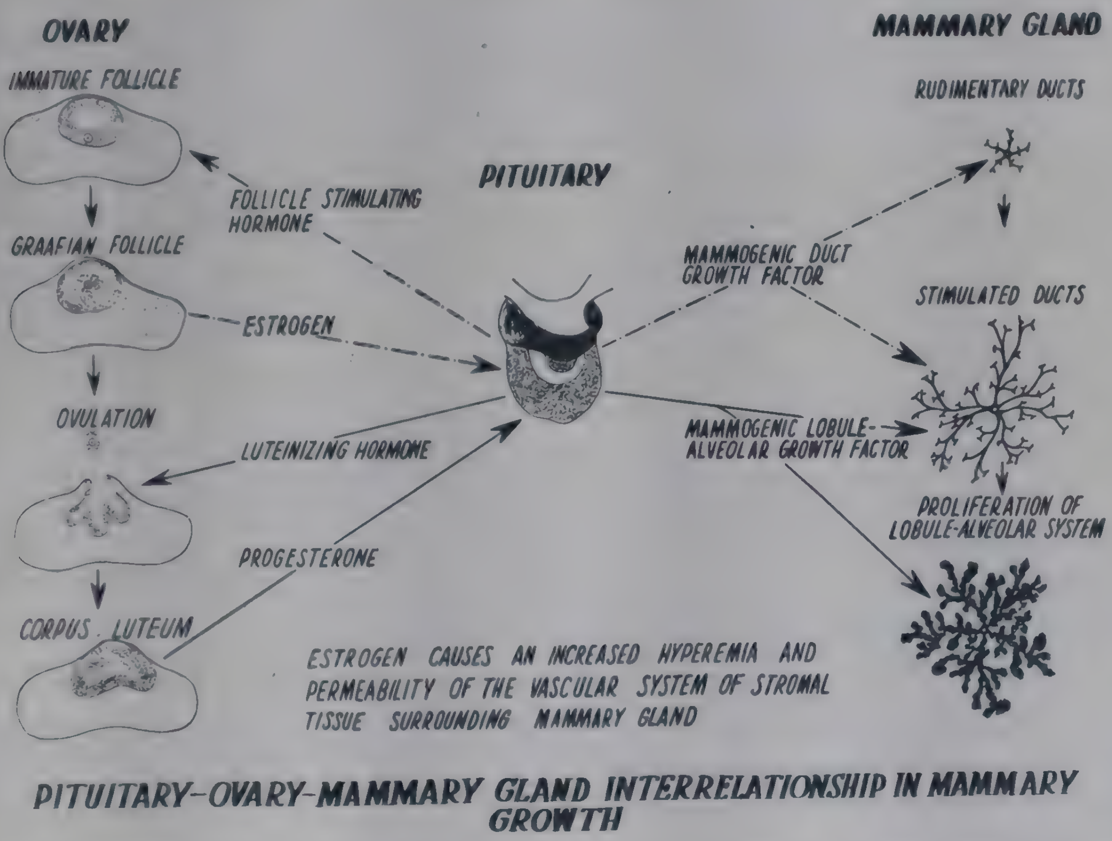
OVARY
IMMATURE FOLLICLE
GRAAFIAN FOLLICLE
OVULATION
CORPUS LUTEUM
FOLLICLE STIMULATING HORMONE
ESTROGEN
LUTEINIZING HORMONE
PROGESTERONE
PITUITARY
MAMMARY GLAND
RUDIMENTARY DUCTS
MAMMOGENIC DUCT GROWTH FACTOR
STIMULATED DUCTS
MAMMOGENIC LOBULE-ALVEOLAR GROWTH FACTOR
PROLIFERATION OF LOBULE-ALVEOLAR SYSTEM
ESTROGEN CAUSES AN INCREASED HYPEREMIA AND PERMEABILITY OF THE VASCULAR SYSTEM OF STROMAL TISSUE SURROUNDING MAMMARY GLAND
PITUITARY-OVARY-MAMMARY GLAND INTERRELATIONSHIP IN MAMMARY GROWTH

Fig. 7.3b—The pituitary in relation to the mammary-gland growth and reproduction. Courtesy J. P. Mixner, and C. W. Turner, Missouri Agr. Exp. Sta.

Returning to Fig. 7.1, not only are male (androgen) and female (estrogen) hormones similar in chemical structure but both are excreted in the urine of males and females. Men excrete about 100 and women about 300 I.U. of estrogen (female hormone) per day. Between 4 and 7 years the estrogen excretion in girls is 8 to 10 I.U. a day; between 7 and 11 years, 20 a day, and about 300 a day thereafter. Boys excrete 20 to 30 I.U. estrogen up to about 14 years, then may increase to 100 (rather than 300 as in girls)[34].

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[34] Nathanson, I. T., Towne, L. E., and Aub, J. C., *Endocrinology*, **28**, 85 (1941). Nathanson and Aub, *J. Clin. Endocr.*, **3**, 321 (1943). Talbot, N. B., *et al.*, *Am. J. Dis. Child.*, **65**, 364 (1943). Greulich, W. W., *et al.*, *Monogr. Soc. Res. Child. Develop. Nat. Res. Council*, **7**, Serial 33, No. 3 (1942); *J. Ped.*, **22**, 518 (1943). The pioneer work is by Gallagher, T. F., and Koch, F. C., *J.A.M.A.*, **108**, 586 (1937) (one woman with "adrenal virilism" excreted 480 capon units of androgen a day as contrasted to 13-79 in normal men and 13 to 50 in normal women).

The androgen (17-ketosteroid) excretion is approximately the same, no only in boys and girls but also in mature men and women[35]. Gonadotropi excretion is about the same in men and w[illegible] n castrated men and post-menopause women[37].

It is curious that bulls and stallions excrete very little androgen (male hormones—far below the amounts excreted by men and women—but stallions excrete enormous amounts of estrogen (female hormone)[38]. The androgen or estrogen excretion may represent metabolic products rather than direct gonadal secretions.

Gonadectomized animals excrete estrogens and androgens. Where are they produced? The adrenal cortex hormones (Fig. 7.1) are chemically similar to sex hormones and the adrenal cortex may produce sex hormones. This is confirmed by changed excretion of these hormones in various diseases of the adrenals. The adrenal-cortex hormone *adrenosterone* shows properties similar to *androsterone*, the active male sex hormone. The adrenal-cortex hormone desoxycorticosterone (sodium-retaining factor) is structurally related to the female sex hormone progesterone, to 21-hydroxyprogesterone; 17-hydroxyprogesterone exerts a physiologic influence similar to the adrenal cortical hormone corticosterone[39].

There is no sharp dividing line between male (androgen) and female (estrogen) hormones structurally (Fig. 7.1) or functionally, as indicated by the stimulating effect of androgens on females, including growth of the uterus and other female sex organs[40], and of estrogens on males[41] (when administered at certain levels under certain conditions). Indeed, even the general design of male and female sex organs is similar, being homologous (same anatomic origin) and analogous (similar physiologic function). Thus the ovary and testes follow a parellel course of development (Fig. 17.4), and sex cannot be differentiated in the embryo until late in development and sometimes not even in late life[42].

This lack of dividing line may also be illustrated by sex inversion in all species. To cite the best known example on a familiar farm animal[43], a young female fowl assumes male characteristics on removal of its left (functional) ovary. Its right ovary is then virtually transformed to a *functional* testicle.

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[5] Aub, *et al*[31]. Scott, W. W., and Vermulen, C., *J. Clin. Endocr.*, **2**, 450 (1943). Koch, F. C., *Biological Symposia*, **9**, 46 (1942).

[36] Varney, R. F., Kenyon, A. T., and Koch, F. C., *J. Clin. Endocr.*, **2**, 137 (1942).

[37] Catchpole, H. R., *et al.*, *J. Clin. Endoc.*, **2**, 181 (1942). Hamilton, J. B., *Anat. Rec.*, **88**, (1944).

[38] Koch, F. C., *Biological Symposia*, **9**, 41 (1942). Doisy, E. A., *Fed. Proc.*, **1**, 202 (1942); *J.A.M.A.*, **116**, 501 (1941).

[39] *Cf.*, Gordon, E. G., *J.A.M.A.*, **114**, 2549 (1940).

[40] Geist, S. H., *J.A.M.A.*, **114**, 1539 (1940); **117**, 2207 (1941). Winterstein, M. P., *Id.*, **116**, 2679 (1941). Salmon, N. J., and Geist, S. H., *J. Clin. Endocr.*, **3**, 235 (1943).

[41] Beach, F. A., *Endocrinology*, **31**, 673, 679 (1942).

[42] For curious anatomic as well as physiologic sex abnormalities, see Young, H. H., "Genital abnormalities", Baltimore, 1937.

[43] *Cf.*, Koch, F. C., ed., *Biological Symposia*, **9**, (1942). For examples of remarkable inversions in birds, see Danforth, C. H., p. 67; in amphibia, Humphrey, R. R., p. 81. Other examples are given by R. R. Greene, p. 105 and Burns, R. K., Jr., p. 123.

rew[44] reported a "normal" fertile hen spontaneously changed to an apparntly "normal" fertile rooster. It is evident that the female at any rate has he potentialities of both in spite of differences in chromosome pattern. nterchanging sex glands in immature male and female rats leads to interchange of sex behavior[45]. Female canaries (non-singing) assume male courtship behavior, including singing, on injecting male hormone[46]. Injecting

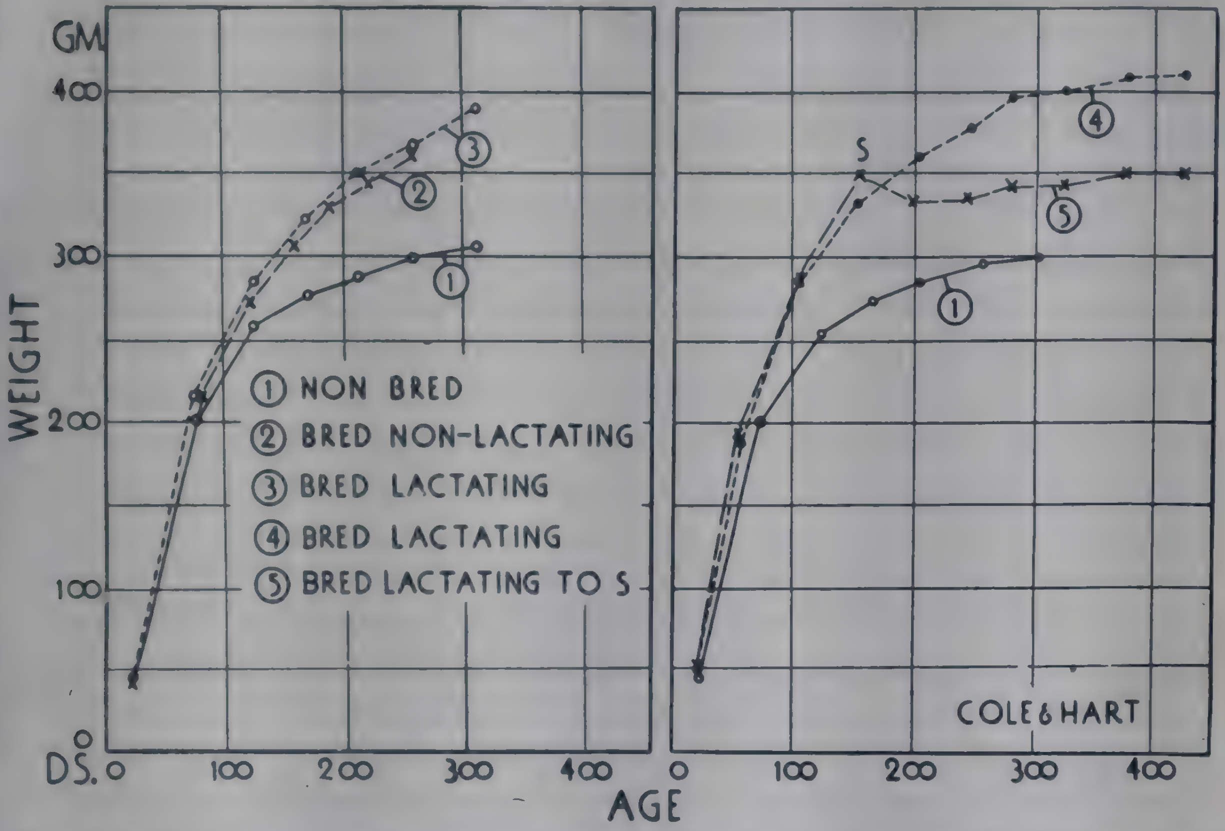

Fig. 7.4—The influence of gestation on growth of rats. Courtesy H. H. Cole and G. H. Hart, *Am. J. Physiol.*, **123**, 589, 1938. Evidently gestation accelerates the growth of the mother.

male sex hormone to females shifts toward male fashion, their muscular development[47], energy metabolism[48], electrolyte picture[49], work capacity[50], and so on[51], including sex behavior[52]. On the other hand, there is considerable difference in growth rate and in other features in males and females aft both have been gonadectomized[53]. There are also prenatal growth differences between the sexes, that is, before sex maturity[54]. Is sex determine by the gonad or is the nature of the gonad determined by the sex of th individual?

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[44] Crew, F. A. E., *Proc. Roy. Soc.*, **95B**, 256 (1923). See also Riddle, O., *Am. Nat.*, **58**, 167 (1924). Zowadowsky, M. M., *Trans. Lab. Exp. Biol.* (Zoopark, Moscow), **4**, 9 (1928).

[45] Stone, C. P., *Endocrinology*, **24**, 165 (1939). Gardner, W. U., *et al.*, *Anat. Rec.*, **75**, 249 (1939).

[46] Leonard, S. L., *Proc. Soc. Exp. Biol. Med.*, **41**, 229 (1929). Baldwin, F. M., *et al.*, *Id.*, **44**, 373 (1940). Fredericks, H. H., *J. Acta. Brev. Neer. Physiol. Pharm. Microb.*, **11**, 24 (1941).

[47] Engle, P., *Endocrinology*, **29**, 852 (1941).

[48] Sandiford, I., *et al.*, *J. Clin. Endocr.*, **1**, 931 (1941).

[49] Kenyon, A. T., *et al.*, *Endocrinology*, **23**, 135 (1938). Korenchevsky, V., *et al.*, *Nature*, **142**, 998 (1938).

[50] Hoskins, R. G., *Am. J. Physiol.*, **72**, 324 (1925). Slonaker, J. R., *Id.*, **112**, 176 (1935), and others by this author. Simonson, E., *et al.*, *Endocrinology*, **28**, 596 (1941).

[51] Pratt, J. P. A., *J. Clin. Endocr.*, **2**, 460 (1942). Witchi, E., *Id.*, **2**, 279 (1942). Allen, E., *J.A.M.A.*, **116**, 405 (1941).

[52] Koster, R., *Endocrinology*, **33**, 337 (1943).

It appears that the urinary steroids may not be functional hormones bu hormonal degradation products. While some hormones, like thyroxine an adrenaline, are known chemical entities, most are known only by their effects Of the many anterior pituitary hormones, only the lactogenic (M.W. abou 25,000) have apparently been obtained in definite purity[55]; and it is not absolutely certain that this hormone, originally called prolactin by Riddle, is th lactation hormone. Indeed, the effect ascribed to a given hormone ma represent the effect of hormonal degradation products, or of several hormones, or perhaps of impurities associated with the hormones rather than of the hormones themselves[56].

There is a pendulum type of oscillation between the pituitary tropic hormones and their controlled endocrines. Thus under condition of stress, the pituitary liberates excessive adrenotropic hormone which induces the adrenal medulla to produce adrenaline. If the the adrenaline production is excessive, it reacts on the pituitary, depressing production of adrenotropic hormones[57]. The periodic sex endocrine activity is an expression of this type of regulation (Sect. 7.2). Similarly, feeding thyroid depresses the production of pituitary thyrotropic hormone and therefore depresses thyroxine production[58]; indeed it atrophies the thyroid. When the blood thyroxine level is reduced, the pituitary again produces thyrotropic hormone and hence thyroxine. Likewise, massive administration of adrenocortical extract depresses cortin production; it atrophies the adrenal cortex[59].

Finally, as explained in Chapter 10, there is a remarkable homeostatic interrelation between the food supply, endocrines, hormones, appetite and related factors. Thus dietary deficiency in iodine leads to compensatory hypertrophy of the thyroid; dietary deficiency in calcium and vitamin D leads o compensatory hypertrophy of the parathyroids. The level of endocrine unction in turn influences food intake, as illustrated by four-fold intake of alcium following parathyroidectomy, two-fold intake of dietary energy following thyroid-hormone or insulin administration, and so on. Hormones and iet are closely interrelated (Ch. 10). A most dramatic interrelation is the nfluence of lack of certain vitamins, especially vitamin E in the rat[60] on pituitary, thus throwing the whole body economy out of gear (Chs. 6 and 20). The interrelations between the hormones and between diet and hormones are closer than most investigators appreciate; hence the apparently contradictory results and claims by different investigators. Any one of an innumerable number of components—hormonal, dietary, or environmental—may become the weak link in the metabolic chain that we call life.

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[53] Hatai, S., *J. Exp. Zool.*, **18,** 1 (1915). Moore, C. R., *Biol. Bull.*, **43,** 285 (1922).

[54] Hill, A. H., *Am. J. Phys. Anthrop.*, **24,** 251 (1939).

[55] White, A., Catchpole, H. R., and Long, C. N. H., *Science*, **86,** 82 (1937). White, Bosnes, R. W., and Long, *J. Biol. Chem.*, **143,** 447 (1932). Li, C. H., Lyons, W. R., and Evans, H. M., *Id.*, **140,** 43 (1941). For recent investigation of adrenocorticotropic and adrenotropic hormones, see Li, Evans, and Simpson, *J. Biol. Chem.*, **149,** 413 (1943), and Sayers, G., White and Long, Id., p. 425. Tyslowitz, R., *Science*, **98,** 226 (1943) obtained corticotropin by dialysis and ultrafiltration of pituitary extract. While it is perhaps protein, its passage through cellophane membrane indicates it to have a much lower molecular weight than prolactin.

[56] Thompson, D. L., Collip, J. B., and Selye, H., *Biol. Rev.*, **15,** 1 (1940); *J.A.M.A.*, **116,** 132 (1941). Thompson, K. W., *Physiol. Rev.*, **21,** 588 (1941). Sulman, F., *J. Exp. Med.*, **65,** 1 (1937).

[57] Selye, H., *J.A.M.A.*, **115,** 2246 (1940) (injecting desocorticosterone acetate and related steroids as progesterone and testosterone involutes the adrenal cortex).

[58] Reforzo-Membrives, J., *Endocrinology*, **32,** 263 (1943).

[59] Ingle, D. J., *et al.*, *Anat. Rec.*, **71,** 363 (1938).

This brings us to the question of whether or not it may be possible to employ hormones for increasing the productive rates and, therefore, the profit on agriculturally productive processes. It is obvious that hormones have two aspects in the efficiency complex. One is illustrated by the extirpation of a gland taking part in a productive process. Thus extirpation of the sex glands reduces the reproductive efficiency to zero; but it does not follow that the converse of this process, namely administration of sex hormones to normal animals, increases the reproductive efficiency. Likewise, removal of the thyroid gland in the young stunts growth and development; yet this does not mean that administration of thyroid hormone to normal young accelerates growth. Similar statements apply to other endocrines. The organismic view point (Ch. 10) leads to the inference that in the struggle for survival in the course of evolution, or even in selection by man, the component parts of the body had to develop so as to function in symphonic harmony of an optimal pattern. Disturbance of this pattern is likely to cause unfavorable after-effects, and therefore reduced efficiency.

However, there are various efficiency aspects, immediate energetic and monetary, and long-range energetic and monetary (Ch. 1). Increase in immediate efficiency is dependent on greater increase in productive rate than in maintenance-cost rate. Increase in long-range efficiency is dependent on absence of unfavorable after-effects sufficiently serious to offset the immediate ain; long-range failure to the *animal* may or may not be associated with ailure to the *animal husbandman.* Thus injurious after-effects which are eveloped in three years will not affect the monetary profit of the animal husbandman if he plans to slaughter the animal within two years. This problem is at present under investigation, and it seems best to study the facts and reserve the judgment.

Under certain conditions hormone administration would definitely be helpful. Thus valuable old animals becoming infertile only because of definitely diagnosed hypothyroidism may be helped by thyroid administration. Th pituitary endocrine action of undernourished animals may be depressed because of the undernourished condition, in which case administration of whol anterior pituitary substance, supplementing a good diet, may be helpful; bu it may not be profitable to do so. In brief, we are not in a position to generalize on this problem at this time.

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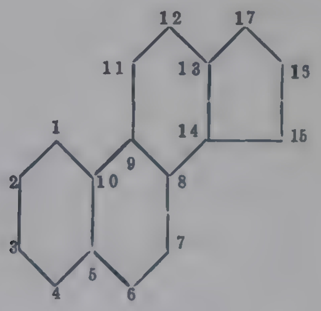
[60] Wieske, B. P., and Bachrach, A. L., *Nature* (Dec. 4, 1937). Barrie, M. O., *Id.*, **139,** 287 (1938). Singer, E., *J. Physiol.*, **87,** 287 (1936). Biddulph, C., and Meyer, R. K., *Am. J. Physiol.*, **132,** 259 (1941).

With the above organismic, or overall, outline of the hormone problem i mind, we proceed to consider some details of each of several endocrine systems The endocrine literature is extremely voluminous and is growing very rapidly This chapter does not attempt to cover the literature, but cites only a few illustrative examples, especially in their bearing on the efficiency complex. The current literature can be followed most easily with the expertly critical reviews in the *Annual Reviews of Physiology*, *Annual Reviews of Biochemistry*, *Physiological Reviews*, *Advances in Enzymology*, and especially the *Journal of the American Medical Association* which emphasizes endocrinal applications as well as the involved theory. Most original researches are reported in *Endocrinology* and in the *Journal of Clinical Endocrinology*.

The following sections are intended to supplement this broad introductory outline of the hormone field.

7.2: Hormones in reproduction and lactation. There is an enormous literature[61] on the endocrines, hormones, and hormonic mechanisms of reproduction, including lactation.

There are many sex hormones, male and female, but, as already noted, they all contain the cyclo-penteno-phenanthrene or the cholesterol nucleus[62] having the formula



which may be considered as a derivative of the three 6-carbon ring phenanthrene, to which is fused the fourth 5-carbon ring.

In its unsaturated form the nucleus offers many points of attachment for side groups in various sequences. This nucleus is, therefore, the mother subance of many compounds, including androgens or male sex hormones (testo-terone, androsterone, and dehydrosterone, the last two probably being uri-ary excretion products of the first); female sex hormones (ovarian follicular ormone variously called estrone, theelin, progynon, menoformen, estradiol, heelol or estriol, equilin, progesterone[63]); corticosterone[64] (hormone from drenal cortex); vitamin D; bile acids; saponins; embryogenic organizers; arcinogens, and so on (Fig. 7.1).

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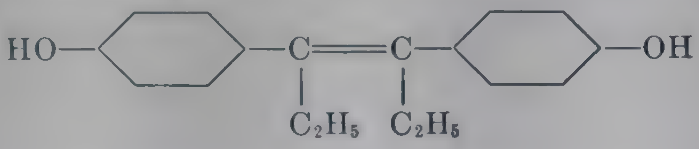
[61] The standard technical work is "Sex and Internal Secretions," by many authors, edited by Edgar Allen, Baltimore, 1939. The most fascinating popular book is "Hormones in Human Reproduction", by G. W. Corner, Princeton Univ. Press, 1942.

[62] *Cf.* Koch, F. C., in Allen[61]; Hopkins, F. G., Dodds, E. C., Parkes, A. S., Ruzicka, L., Cook, J. W., Reichstein, T., and Todd, A. R., "Synthetic organic chemistry in biology and medicine", *Nature*, **142,** 524 (1938). Fieser, L. F., "Chemistry of natural products related to phenanthrene", New York, Reinhold Publishing Corp., 1937, and *Am. J. Cancer*, **34,** 37 (1938). Bills, C. E., *Physiol. Rev.*, **15,** 1 (1935); "Quantitative Biology", Vol. 5, 1937.

The chemical differences in the various sex hormones are due mostly to differences n substitutions in positions 3, 5, 17 in the above nucleus, and in stereochemical con-iguration. The difference between estrone and progesterone is that the former has an IO— in position 3, the latter an O═and by some minor differences in positions 10 and 17. The difference between testosterone and progesterone is only in position 17: Pro-gesterone has the $CO \cdot CH_3$ group, testosterone the $H \cdot OH$ group. The difference be-tween corticosterone and progesterone is that the former, but not the latter, has an OH in position 1 and in position 17; corticosterone has an $CO \cdot CH_2OH$ group, while progesterone, a $CO \cdot CH_3$ group. Indeed, corticosterone exhibits progesterone-like activity[65]. It is impressive to contrast the unity of basic structure and *ultimate* func-tion, with the diversity in immediate function.

While the natural sex hormones are built about the phenanthrene nucleus, a synthetic strogen, diethyl stilbestrol ("stilbestrol"), synthesized by Dodds[66], namely,



which does not contain the phenanthrene ring, is at least twice as potent[67] an estrogen as the natural estrogen estrone. The formula of stilbestrol may be rearranged to appear like estrone with two incompleted positions. This does not, however, work out with 3-dimensional models.

An enormous literature on stilbestrol has grown up[68] since the appearance of the paper by Dodds, Goldberg, Lawson and Robinson in 1938. Stilbestrol has remarkable growth-stimulating properties on the uterus of immature rats and on the mammary gland[69, 70], and has lactation-initiating properties[70]. Stilbestrol, however, depresses lactation after it is established[71]. The effect of the stilbestrol is assumed to be by way of the pituitary. More recently another synthetic estrogen, octofolin[72] (a phenyl-ethyl hexane), less toxic for a given estrogenic effect than stilbestrol has come into use[73].

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[63] Progesterone appears to be androgenic. Clausen, H. J., *Endocrinology*, **31**, 187 (1942). There is some antagonism between estrogen and progesterone as presently explained.

[64] Wintersteiner, O., and Smith, P. E., *Ann. Rev. Biochem.*, **7**, 253 (1938).

[65] Robson, J. M., *J. Physiol.*, **95**, 83 (1939).

[66] Dodds, E. C., Goldberg, L., Lawson, W., and Robinson, R., *Nature*, **141**, 247 (1938).

[67] MacBryde, C. M., Dreedman, R., Doeffel, E., and Castrodale, D., *J.A.M.A.*, **115**, 440 (1940).

[68] "Diethylstilbestrol" (annotated bibliography), Merck & Co., Rahway, N. J., 54 pages, October 1940.

[69] Jacobsen, E., and Skaarpp, C. S., *Acta Path. Microb. Sci.*, **16**, 359 (1939).

[70] Folley, S. J., Watson, H. M. S., and Bottomley, A. C., *J. Physiol.* (May 14, 1940) p. 15 (1 per cent ointment was applied thrice weekly to the udder of a virgin goat. After a 30-day latent period, milk production increased to 1500 cc per day, the lactation curve resembling a normal lactation curve). Lewis, A. A., and Turner, C. W., Paper presented before the Am. Soc. Animal Prod. Nov. 28, 1940, and *Endocrinology*, **31**, 520 (1942). Stilbestrol stimulated rapid growth of the mammary duct system comparable to that caused by natural estrogen. Lactation was induced in goats up to 600 cc.

The *chemistry* of the sex hormones thus appears simple in general design. The *physiology* of the sex cycle differs with the species: some breed only during certain seasons (Ch. 8), others only at approximately monthly cycles, still others at 5-day cycles, and so on. We are most familiar with the monthly and shorter cycles[74] in non-seasonal breeders.

As previously noted, the female sex cycle is controlled by the interplay between two classes of hormones: (1) the pituitary or gonadotropic hormones, which stimulate the ovary to produce estrogenic hormones; (2) the estrogenic hormones produced by the ovary under the influence of the pituitary gonadotropic hormones. These estrogenic hormones depress the pituitary production of gonadotropic hormones; the activating stimulus for the ovary to produce estrogens is thus removed. In this way there is brought about an oscillatory or periodic cycle of high pituitary gonadotropic hormone production and high ovarian estrogen production. This cycle continues from puberty until the menopause[75], when the ovary ceases to respond to the high gonadotropic hormone. Gonadectomy in either sex, or absence of sexual development, is associated with a permanent elevation of gonadotropin excretion[76].

The estrogenic hormones are very concentrated in the egg follicles (ovarian and graafian follicles). Allen and Doisy (1922) injected the fluid from these follicles into castrated mice and rats, bringing about the cycle without the presence of the ovary. The course of the cycle is followed most easily by changes in the appearance of the vaginal smear (Stockard and Papanicolaou, 1917) and is used for estimating the potency of the estrogen hormone (Edgar Allen and Doisy, 1922). This method for assay of the hormone led to its ever greater purification and final isolation (Doisy, 1929).

The steps in the estrus cycle are roughly as follows:

(1) Beginning with puberty, the pituitary (gonadotropic hormones) activates the ovary (and perhaps other tissues) to produce estrogen hormones

(2) The estrogen hormones stimulate growth of most sex organs, especially the ovarian (graafian) or egg follicles, ripening of the eggs, ovulation, *i.e.*, shedding of the eggs from the ovarian follicles, and the phenomenon of estrus[77]. Estrus is what farmers call heat, or sexual receptivity, when fertilization may occur.

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[71] Turner, C. W., and Mixner, J. P., unpublished data.

[72] Blanchard, W. W., *et al.*, *Endocrinology*, **32,** 307 (1943).

[73] Hufford, A. R., *J.A.M.A.*, **123,** 259 (1943). Roberts, H. K., *et al.*, *Id.*, p. 261.

[74] *Cf.* Guthrie, Mary J., "Reproductive cycles in animals," *Growth*, **3,** 261 (1939).

[75] Sub-human or sub-anthropoid species, apparently, do not have a menopause (sudden cessation of reproductive activity); the reproducing ability seems to decline gradually until the end of life. Also human males do not appear to have a sudden climacteric comparable to the menopause in women, but a gradual decline.

[76] Varney, R. F., *et al.*, *J. Clin. Endoc.*, **2,** 137 (1942). Albright, F., *et al.*, *Am. J. Med. Sci.*, **204,** 625 (1942). Heller, C. G., *et al.*, *J. Clin. Endoc.*, **3,** 573 (1943).

[77] "Estrus (or oestrus) means 'periodic sexual excitement of the female,' but estrum means *any* recurrent excitement," G. W. Corner, *Science*, **85,** 197 (1937).

(3) After the eggs are shed from the egg follicles, the latter become endorine organs called corpus lutea, producing another hormone, progesterone, which controls the implantation and nourishment of the fertilized egg in the uterus, including formation of the placenta.

(4) If no fertilization occurs, this growth of the uterine bed degenerates, and this whole elaborate receptional structure for the fertilized egg is swept out. In man and most anthropoids, this sweeping out, called menstruation, s dramatic because of the hyperemia and bleeding of the endometrium (lining of the uterus). In other species, it passes unnoticed, without bleeding; these species do not menstruate. It is curious that those species that have a marked estrus do not have marked menstruation, and conversely.

Women have menstruation, that is, a visible bleeding, or sweeping out of the receptional set-up in the uterus, but no estrus, that is, no sexual excitement at the time of ovulation. They are, indeed, unaware of the time of occurrence of ovulation[78]. Ovulation in women usually occurs sometime between the eighth and twentieth day after the beginning of menstruation, when fertilization can occur. In farm and laboratory animals other than anthropoids, fertilization can occur only during estrus, that is, during sexual excitement, which coincides with ovulation.

If the egg is not fertilized, the decline of estrogen hormone production by the ovary releases the pituitary to produce more gonadotropic hormone, and the whole elaborate sex cycle is repeated.

This brief outline illustrates the balance between the gonadotropic and estrogen hormones. The cyclic nature of sex activity is thus a pendulum-like oscillation between pituitary and ovarian activity. This discussion also illustrates the general design and sequence of the processes: egg follicle becomes the corpus luteum after the discharge of the egg, and this structure, which previously produced estrogen (in the follicular solution) for producing estrus in the *female*, now produces progesterone for producing the housing facilities for the *young*. Though differing in function, the progesterone is chemically similar to estrogens and androgens; by a slight change the same material serves as estrogen, as progesterone, as androgen, and as one of several other hormones (Fig. 7.1).

But this is not all. When the infant is born it has to be nourished; thus it comes about that at puberty, when the ovary becomes sensitized to the pituitary gonadotropic hormone and produces estrogen hormones, the estrogen, which is instrumental in maturing the sex organs and ripening the eggs, also acts on the mammary gland causing it, especially the duct system, to grow rapidly. The development of the mammary gland, the apparatus for *nourish-*

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[78] See, however, Rosenzweig, S., *J. Clin. Endocr.*, **3**, 296 (1943), indicating shifting psychic attitudes from the pre- to the post-ovulative phase. For cyclic temperature and metabolism changes, see Rubenstein, B. B., *Endocrinology*, **22**, 41 (1938). For an electrometric method of timing human ovulation, see Langman, L., and Burr, H. S., *J. Heredity*, **33**, 223 (1942). Too many factors, however, influence the electric potential difference to make it significant [Snodgrass, J. M., *Am. J. Physiol.*, **140**, 394 (1943)].

ing the young, is thus synchronized with that of the sex organs, the apparatus for *producing* the young.

The milk-secreting alveoli (terminal-chamber) stage of the mammary gland is perfected during gestation under the influence of the progesterone hormone, the same hormone which controls the production and maintenance of the reception and nutritional chamber for the embryo. It should be noted that the effects of the various hormones are confined to specific tissues at definite ages, in definite states of competence to react to the given hormones. The "logistics"—to employ a current military term—of this process thus appear to be, so to speak, arranged with foresight, economy, and the ultimate in perfection of timing. One is tempted to carry the logistics of this reproductive campaign both backward, to the emotional (neuro-psychologic) mechanisms which bring male and female together with all the familiar courtship devices and all the far-reaching social implications, and forward not merely to the production of milk, but also to the development of maternal behavior, found in mice as well as men. These emotions are apparently under the control of neuro-endocrine mechanisms[78a]. It is interesting to note that in some species, pigeons for example, milk production (pigeons produce about 10 g "pigeon milk" a day similar in composition to rabbit milk—65 to 80 per cent H_2O, 13 to 19 per cent protein, 7 to 13 per cent fat, 1.5 per cent ash) and brooding are shared by both parents, and that for their proper functioning the male must have testes as females must have ovaries. The gonadotropic hormones are probably the same in male and female, and, as noted, the testicular hormones differ only ln detail from the ovarian sex hormones.

The discovery that ovarian activity is controlled by anterior-pituitary hormones was made by Smith and Engle[79] and Zondek and Ascheim[80]. This pituitary control of gonadal activity is demonstrated by: (1) hypophysectomy, which is followed by cessation of sex function, and restoration by pituitary implants[81]; (2) naturally sterile dwarfs (mice) become fertile on pituitary implantation[82]; (3) implantation of mature pituitary tissue[83] or injecting gonadotropic preparation[84] (or testosterone proprionate[85]) in infant chicks or rats results in extreme sex precocity (sex "maturity" in 15-day old mice or 10-day old chicks). Cushing[86] observed some thirty years ago that hypophysectomy is followed by atrophy of the gonads.

So many hormones are referred to the anterior lobe that one wonders whether there are special tissues that secrete each of the hormones. Warbritton and McKenzie[87] reported the recognition of nine morphologically different types of cells in the glandular lobe of the anterior pituitary of the ewe[88]. The anterior pituitary appears to have (1) chromophobe cells which do not stain well, and (2) chromophil cells which do stain well. Of the latter, there are (2a) acidophil cells which stain by acid dyes, and (2b) basophil cells which stain by basic dyes. The lactogenic and growth hormones are attributed to the acidophils, the gonadotropic to the basophils. The growth-hormone production is attributed to the acidophils because of their absence in dwarf-mice[89] pituitaries and their overabundance in "giants"[86].

[78a] Riddle, O., *Proc. Am. Phil. Soc.*, **75**, 521 (1935).

[79] Smith, P. E., *Proc. Soc. Exp. Biol. Med.*, **24**, 131 (1926); Smith and Engle, E. T., *Am. J. Anat.*, **40**, 159 (1927).

[80] Zondek, B., and Ascheim, S., *Arch. Gynak.*, **130**, 1 (1927).

[81] Smith, P. E., *Proc. Soc. Exp. Biol. Med.*, **24**, 337 (1927); *J.A.M.A.*, **88**, 158 (1927); *Am. J. Anat.*, **45**, 205 (1930).

[82] Smith, P. E., and MacDowell, E. C., *Anat. Rec.*, **46**, 249 (1930); **50**, 85 (1931).

[83] Smith, P. E., *Proc. Soc. Exp. Biol. Med.*, **24**, 131 (1926); *Am. J. Physiol.*, **80**, 114 (1927); Engle, E. T., *Am. J. Physiol.*, **88**, 101 (1929); *Endocrinology*, **15**, 405 (1931); **16**, 506 (1932). For age of normal sexual maturity in mice, see Engle, E. T., and Rosasco, J., *Anat. Rec.*, **36**, 383 (1927).

[84] Domm, L. V., and Van Dyke, H. B., *Proc. Soc. Exp. Biol. Med.*, **30**, 349 (1932).

[85] Hamilton, J. B., *Endocrinology*, **23**, 53 (1938).

[86] Cushing, H., "The pituitary and its disorders," 1912.

As previously outlined, under the influence of the pituitary gonadotropic hormones, the gonads (testis, ovary) produce sex hormones which control the growth of sex tissues, including mammary gland, secondary sex characteristics, and sex functions in general. The male (testis) hormones are the androgens; the female (ovarian) hormones are of two kinds: (1) estrogens produced mostly in the ovarian follicles, controlling the estrus cycles, including ovulation and mating, and (2) progesterone produced by the corpus luteum, controlling implantation and nutrition of the fertilized ovum. The estrogens are produced under the influence of the (pituitary gonadotropic) follicle-stimulating hormone, or F.S.H.; progesterone is produced under the influence of the (pituitary gonadotropic) luteinizing hormone, or L. H., identical with I.C.S.H. (interstitial cell-stimulating hormone).

The terminology of the sex hormones is involved[90], as indicated by the following outline, which is by no means generally accepted.

The known female sex hormones are: (1) *estradiol*, the active estrogen principle in the ovaries; (2) *estrone*, or theelin, produced from estradiol in the ovaries, is found in blood and urine in males as well as in females (corpus luteum, placenta); (3) *estriol*, or theelol, produced from estrone in the uterus (the conversion does not occur in the ovariectomized), constitutes about 80 per cent of the estrogen in pregnant urine; (4) *equilin*, and its isomers hippulin and equilenin, have thus far been found in mare urine only.

Assays for sex hormones are growth responses of specialized tissues. Thus the Corner-Hisaw test for progesterone is the growth response of the uterine endometrium; the Allen-Doisy test for estrogen is a growth response of the genital tract including estrus production; the Koch test for male sex hormones is the growth response of comb and wattles of the capon. A test of another category is that for acetylcholine which estrogens release in the uterus. The latest pregnancy test[91] in humans consists in administering prostigmine, which activates the acetylcholine and leads to hyperemia and consequently induces menstrual flow provided the subject is not pregnant.

It was noted that the placenta produces gonadotropic hormone. The time curve of its production with the advance of the period of gestation has been worked out for cattle[92] and women[93]. The following, for women[93], is timed from the first day that the menstrual period is missed.

Days	3	14	22	36	46	55–66	80	99	4 days after birth
Urinary Hormone per day	150	65,000	125,000	1,040,000	260,000	130,000	65,000	10,400	0

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[87] Warbritton, V., and McKenzie, F. F., Univ. Missouri Agr. Exp. Sta. Res. Bul. 257, 1937.

[88] Schooley, J. P., and Riddle, O., "The morphologic basis of pituitary function in pigeons", *Am. J. Anat.*, **5,** 313 (1938).

[89] Smith, P. E., and MacDowell, E. C.[82] (1930).

[90] Frank, R. T., *J.A.M.A.*, p. 1504 (April 20, 1940).

[91] Carapetyan, H., *J.A.M.A.*, **122,** 81 (1943).

[92] Turner, C. W., Frank, A. H., and Nibler, C. W., Univ. Missouri Agr. Exp. Sta. Res. Bull. 150, 1930.

[93] Evans, H. M., *et al.*, *J.A.M.A.*, **108,** 287 (1937).

The Ascheim-Zondek pregnancy test previously explained is a test for these urinary gonadotropins. The function of the placental gonadotropins, perhaps, is to stimulate the corpora lutea.

As regards lactation, Grüeter and Stricker[94] in Strasbourg and Corner[95] in this country demonstrated that this process is under the control of the pituitary.

Some investigators[94] maintain that milk secretion is the resultant of the action of a series of *distinct* pituitary hormones: (a) lactogenic, which regulates milk production *by direct influence on the secreting cells* of the mammary gland, and (b) several metabolic hormones for protein, carbohydrate, fat, etc., each of which regulates milk production by its *influence on a particular milk precursor*. Other investigators[96] maintain that the same biochemical entity which stimulates milk secretion by mammary cells, *i.e.*, the lactation hormone, also shows other hormonal properties, among which may be: (1) calorigenic in conjunction with the pituitary thyrotropic hormone; (2) calorigenic in thyroidectomized animals; (3) diabetogenic[97]; (4) crop-secretion stimulant in pigeons; (5) releaser of brooding instinct in fowls and maternal behavior in rats[98], sustainer of liver, pancreas, and intestines in pigeons; (6) participator in acceleration of growth. However, these may be due to impurities associated with the lactogenic hormone. The "lactation hormone" is customarily assayed by its influence on crop gland growth[99] in pigeons of either sex rather than by its milk-stimulating property. The theory that the same substance which stimulates mammary-gland cells to produce milk also induces maternal behavior gives a functional unity to a diversity of phenomena.

The mechanism of mammary-gland growth is at present under investigation. The following notes represent the ideas of my department colleagues[100] as summarized in Fig. 7.3b. The mammary gland is made up of several components, including the stromal connecting tissues which house the vascular system and glandular tissue, and the parenchymatous tissue (ducts, alveoli, lobules, etc.)—the milk-conducting and -secreting tissues.

As regards the parenchymatous tissues, at birth they usually consist of the primary ducts from which secondary ducts have sprouted. The mammary duct tree develops during the recurring estrous cycles of puberty while the mammary lobule-alveolar system (terminal-chamber secreting system) develops during the first half to two-thirds of pregnancy. The hypertrophy of the gland preceding parturition is not due to growth but to swelling with secretion. There is apparently little growth of the gland during lactation, unless pregnancy occurs simultaneously, in which case there may be additional gland growth.

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[94] Turner, C. W., in Edgar Allen's "Sex and Internal Secretions."

[95] Corner, G. W., in Edgar Allen's "Sex and Internal Secretions."

[96] Riddle, O., *Cold Spring Harbor Symposia on Quantitative Biology*, **5**, 218 (1937); Ann. Rep. Dir. Dept. Genetics, Carnegie Institution of Washington, pp. 52–62, December 1937; also *Sci. Monthly* (August, 1938).

[97] However, Bergman and Turner reported [*Endocrinology*, **22**, 619 (1938)] chemical separation of lactogenic and carbohydrate-metabolism anterior-pituitary hormones. Also, Bergman, A. J., and Turner, C. W., *J. Dairy Sci.*, **23**, 1229 (1940).

[98] Riddle[96]. However, Leblond and Nelson [*Am. J. Physiol.*, **120**, 167 (1937)] reported maternal behavior in hypophysectomized animals.

[99] Bates, R. W., *Cold Spring Harbor Symposia on Quantitative Biology*, **5**, 191 (1937). Lyons, W. R., *Symposia on Quantitative Biology*, **5**, 198 (1937). The discovery of this crop test and that the pituitary extract that contains the lactogenic hormone is identical with the extract that gives this crop test are due respectively to Riddle, O., and Braucher, P. F., *Am. J. Physiol.*, **97**, 617 (1931), and Riddle, Bates, R. W., and Dykshorn, S. W., *Id.*, **105**, 191 (1933). Riddle named this pigeon-crop factor "prolactin". Others named it later galactin, lactogen, lactogenic hormone, mammotropin, and so on. One cannot be certain of the role of this factor in milk production, since milk production is dependent on many interrelated hormones, for example, thyroxine and cortin factors.

[100] Mixner, J. P., and Turner, C. W., Univ. Missouri Agr. Exp. Sta. Res. Bull. 378, 1943. C. W. Turner in Edgar Allen's "Sex and Internal Secretions". Riddle, O., *J.A.M.A.*, **115**, 2276 (1940).

It is now generally believed that mammary growth is under direct pituitary control. Corner[101] was the first to report that he observed development of the mammary glands of young castrated rabbits under the influence of injections of an alkaline extract of sheep anterior pituitary. Turner *et al.*[102] first demonstrated that the presence of the pituitary is essential for mammary growth, the ovarian hormones being ineffective in the absence of the pituitary. The present theory, based on research in the Missouri laboratory, is that estrogen (during puberty and estrus) stimulates the pituitary to an increased secretion of a mammogenic duct-growth hormone, whereas progesterone (during gestation) stimulates the pituitary to an increased secretion of a mammogenic lobule-alveolar-growth factor. Estrogen causes an increased hyperemia and vascularity of the stromal tissue associated with an increased permeability of the vascular system[103]. Thus more rapid growth of the mammary gland is promoted indirectly by increasing the amount of pituitary mammogen and nutrients present in the intercellular spaces in the region of the mammary gland. This action of estrogen explains the so-called "local action" of estrogen in promoting mammary growth reported by Lyons[104], Speert[105], and others. This action of estrogen is dependent upon the presence of a circulating pituitary mammogen.

Summarizing, while the rate of mammary growth may be influenced by many factors (for example the thyroid and adrenals), the mammary gland is the specific target gland of the pituitary. The ovarian hormones, estrogen and progesterone, act on the pituitary to stimulate increased amounts of mammogenic factors. Estrogen in addition causes an increased hyperemia and permeability of the vascular system.

The mammogenic hormones are protein in nature. Their possible identity with other pituitary hormones has not been fully investigated, although it is probable that the lobule-alveolar-growth factor is not the same as lactogen, thyrotropin, or gonadotropin.

As regards the mechanism which initiates lactation, it appears[106] that estrogen is the primary stimulator of the lactogenic hormone produced by the pituitary. During pregnancy progesterone checks the estrogen action. At parturition progesterone production decreases, the inhibiting effect on estrogen is removed and lactation proceeds. Once lactation is established, the stimulus of suckling or milk removal reflexly stimulates the periodic release of lactogenic hormone from the pituitary.

It is not possible to discuss the influence of prolactin administration on the efficiency of milk production. All that we know is that injection of a crude extract[107] of the anterior pituitary gland, and in some cases stilbestrol, may show, among other effects, initiation of milk production[108].

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[101] Corner, G. W., in Edgar Allen's, "Sex and Internal Secretions", and *Am. J. Physiol.*, **95**, 43 (1930).

[102] Gomez, E. T., Turner, C. W., and Reece, R. P., *Proc. Soc. Exp. Biol. Med.*, **36**, 286 (1937).

[103] Mixner and Turner[100]

[104] Lyons, W. R., *Proc. Soc. Exp. Biol. Med.*, **44**, 398 (1940).

[105] Speert, H., *Science*, **92**, 461 (1940).

[106] Meites, J., and Turner, C. W., *Endocrinology*, **30**, 711, 719, 726, 340 (1942).

[107] White, A., Catchpole, H. R., and Long, C. N. H., "A crystalline protein with high lactogenic activity", *Science*, **86**, 82 (1937). The lactogenic activity of the crystalline product does not exceed that of the cruder extracts generally employed.

[108] Turner[100], Asimoff, G. J., and Krouze, N. K., "Lactogenic preparations from the anterior pituitary and the increase of milk yield in cows", *J. Dairy Sci.*, **20**, 289 (1937). Folley, S. J., and Young, F. G., "Stimulation of milk production by prolactin in the cow," *J. Soc. Chem. Ind.*, **56**, 96 (1937). Kay, H. D., "The biochemistry of milk secretion", *J. Roy. Soc. Arts*, **85**, 841 (1937), and others.

7.2.1: Some applications of sex endocrinology. The evolutionary and agricultural advantage of this complex process of sexual reproduction—as contrasted to asexual and other simpler reproductive methods not involving the complex neuro-endocrine mechanism (see Sections 10.8 and 10.9)—is that it promotes most diversification in the offspring. This favors the best evolutionary and agricultural selection, or "survival of the fittest", under the given environmental conditions. The improved breeds of farm animals and plants were, of course, achieved by such selection from variant individuals, each a carrier of highly diverse genes.

A curious feature of some practical importance is the difference in sex mortality. In man, at any rate, the male mortality is consistently above that of the female, and the same appears to hold for other mammals. One possible explanation for the higher male mortality is that the (maternal) female hormones may exert a lasting injury on the male offspring during his physiologically prolonged sojourn *in utero*, that is, assuming an antagonism between female and male hormones.

That there may be an antagonism between male and female sex hormones (depending on dosage) is indicated by the fact[109] that of the twin calves of opposite sex, the female (called "free martin") seems to lose her sex function permanently by prenatal commingling of the blood of the two sexes. Pituitary gonadotropins are produced prenatally, as indicated by the sex-stimulating effect of fetal pituitaries[110]. There is other evidence of sex-hormone antagonism, as indicated by atrophy of male genitals by injecting large amounts of female hormone[111]. However, the male organs are also injured by injecting male sex hormone[112].

It is more reasonable to attribute the higher mammalian male mortality to his constitutional difference—to his having one unpaired or X-chromosome. It is generally known that there are two kinds of mammalian sperms, female-producing, having paired or even number of chromosomes, and male-producing, having unpaired or odd number of chromosomes (the opposite is true for birds and butterflies). Mammalian males having only one, the X-chromosome, carry as dominant some characters which in the female are masked by the complementary genes in the Y-chromosomes. Some of the unmasked characters, such as hemophilia, are very dangerous in the male but harmless in his mother because of protection by the complementary Y gene in the female chromosome. Color blindness and baldness are well-known harmless dominants in men which are recessive in women.

The literature on the influence of experimental manipulation of sex-hormone level on growth and development is large and confused because it varies with species, race or family within the species, individuals within the family, sex, age, length of time of hormone administration, period following the hormone administration, hormone dosage, diet, and so on.

By way of introduction it may be recalled that, in general, development or maturation is more rapid in females than in males[113]; also that breeding females often grow to be larger than non-breeding[114]. The results on human growth (see Fig. 16.62, the ratio of the growth rate of girls to boys) are in agreement with those on other mammals. Ossification tends to be somewhat more rapid in girls than in boys, even during prenatal and prepubertal life[115] and the onset of puberty accentuates these differences[116]. The differences between the sexes evidently are partly genetic, and independent of the sex hormones, since, as previously explained, there are prenatal and prepubertal developmental differences which extend to differences between early gonadectomized males and females; there are also sex differences resulting from hormonal action, since the pattern of sex behavior in each sex, especially in the female, is influenced by administration of sex hormone from the opposite sex.

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[109] Newman, H. H., "Twinning", Univ. Chicago Press, 1923-4.

[110] Smith, P. E., *Anat. Rec.*, **43**, 277 (1929).

[111] Matthews, C. S., *et al.*, *Endocrinology*, **29**, 761 (1941).

[112] Wilson, J. G., and H. C., *Id.*, **33**, 353 (1943).

[113] *Cf.*, among many others, Latimer, H. B., *Anat. Rec.*, **40**, 1 (1927); Sparks, C. A., and Dawson, A. B., *Am. J. Anat.*, **41**, 411 (1928). Silberberg, M. and R., *Endocr.*, **29**, 475 (1941); **31**, 410 (1942).

[114] Slonaker, J. R., *Am. J. Physiol.*, **82**, 318 (1927). Cole, H. H., and Hart, G. H., *Am. J. Physiol.*, **123**, 589 (1938). Bogart, R., *et al.*, *Id.*, **128**, 355 (1940). Silberberg, M. and R.[112]

The foregoing introduction may be useful in interpreting the experimental data on the effects of gonadectomy and sex-hormone administration.

Estrogen administration to normal females for considerable periods tends to inhibit growth of the long bones, thereby retarding growth[117]. Precocious sexual maturity in girls is often associated with short legs[118]; on the other hand, excessive limb growth has been checked by estrogen administration[119]. Estrogen administration to growing mice increased the breaking strength of bones[120] but did not affect the bone length[121].

The influence of sex-hormone administration or removal may be by the intermediacy of the pituitary[122] and thyroid[123], which lead to rate differences in epiphysial closure, ossification of the bone matrix[124], aging of cartilage[125], and so on[126].

Progesterone tends to neutralize the estrogen effects[127]. While estrogen depresses the growth rate, progesterone stimulates it[127]. This may explain the fact that pregnancy stimulates the growth of the mother[128] despite the increased estrogen production at that time.

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[115] Hill, A. H., *Am. J. Anthrop.*, **24**, 251 (1939).

[116] Greulich, W. W., *Am. J. Phys. Anthropol.*, **27**, 13 (1940); *Endocr.*, **30**, 1023 (1942). See also, Pryor, J. W., *Anat. Rec.*, **25**, 257 (1923). Francis, C. C., *Am. J. Phys. Anthrop.*, **27**, 817 (1939). Bunak, V., *Id.*, **26**, 69 (1940).

[117] Spencer, J., Gustavson, R. G., and d'Amour, F. E., *Proc. Soc. Exp. Biol. Med.*, **28**, 500 (1931); *Am. J. Anat.*, **50**, 129 (1932). Zondek, B., *Lancet*, **2**, 842 (1936); *Am. J. Cancer*, **33**, 555 (1938).

[118] Reilly, W. A., *Endocrinology*, **18**, 117 (1934). Bayer, L. M., *Id.*, **24**, 260 (1939).

[119] Goldzieher, M. M., *J. Clin. Endocr.*, **1**, 924 (1941).

[120] Gardner, W. U., Endocr., **32**, (1943); *Physiol. Rev.*, **21**, 193 (1943).

[121] Silberberg, M. and R., *Am. J. Anat.*, **69**, 295 (1941).

[122] Evans, H. M., and Simpson, M. E., *J.A.M.A.*, **91**, 337 (1928); *Am. J. Physiol.*, **98**, 511 (1931). Zondek, B., *Lancet*, **1**, 10; **2**, 842 (1936). Rubinstein, H. S., *et al.*, *Endocrinology*, **25**, 397, 724 (1939).

[123] Kippen, A. A., and Loeb, L., *Endocr.*, **20**, 201 (1936).

[124] Gardner, W. U., *Physiol. Rev.*, **23**, 139 (1943).

[125] Silberberg, M. and R., *Anat. Rec.*, **78**, 459 (1940); *Endocr.*, **29**, 475 (1941).

[126] Goldzieher[119], McCullagh, E. P., and Rossmiller, H. R., *J. Clin. Endocr.*, **1**, 507 (1941); *J.A.M.A.*, **116**, 2530 (1941). Turner, H. H., *et al.*, *Endocr.*, **29**, 425 (1941). Richards, R. R., and Keuter, K., *Id.*, **29**, 990 (1940). Albert, S., *Id.*, **30**, 454 (1942). Finkler, R. S., *et al.*, *J. Clin. Endocr.*, **2**, 603 (1942).

[127] Bogart, R., *et al.*, *Am. J. Physiol.*, **128**, 355 (1940); *J. Agr. Res.*, **60**, 847 (1940). Silberberg, M. and R., *Arch. Path.*, **31**, 85 (1941); *Endocr.*, **29**, 475 (1941); **31**, 410 (1942). Gilman, J., and Stein, H. B., *Endocr.*, **31**, 187 (1942). Gardner[124].

Gonadectomy in males is usually followed by immediate growth retardation, although ultimate growth acceleration may result[129]. Gonadectomy of females on the other hand is usually followed by immediate growth acceleration, although there may be later growth retardation[130].

Ovariectomy probably stimulates growth by removing the growth-inhibiting effect of estrogen, although not as much as gestation[131]. The effect depends on the age of ovariectomy. Freudenberger[132] ovariectomized 47-g rats at age 4 weeks At the age of 6 weeks the ovariectomized rats weighed 4 per cent more, at 7 weeks 8 per cent, and at 13 weeks 20 per cent more than the normal controls (the ovariectomized rats weighed 205 g; the controls 171 g) The visceral-organ weights of the ovariectomized rats were greater than those of the control by 77 per cent for thymus, 23 per cent for spleen, 18 per cent for pituitary, 17 per cent for lungs and digestive tract, 13 per cent for heart and liver, 10 per cent for thyroid and adrenals, 8 per cent for kidneys, and 4 per cent for body and tail length.

While early gestation stimulates growth and increases the mature size of the mother (Fig. 7.4), early breeding of dairy cattle[133], swine[134], and sheep[135] retards growth because of the drain of heavy lactation (not gestation). Early-bred heavily-lactating animals usually reach normal size but at a later age, requiring a longer period to attain normal size. Early-bred heavily lactating rats invariably reach normal size, often super-normal size[136], if properly fed.

Cole and Hart[137] bred young rats and found no harmful effect of lactation on the growth of the immature mothers. However, the litter size was reduced at birth to 4 to 6 young, and the mothers had access to an excellent diet. The average litter size in this strain of rats was reported to be 11.5 with a range of 1 to 19. These investigations report remarkable growth acceleration (by about 16 per cent over the controls) of the mothers by frequent pregnancies. The growth-accelerating effects of pregnancy on the mothers were interpreted to mean that pregnancy stimulates the pituitary to secrete growth hormones. "Pregnancy is intermediate in its growth stimulus between that occurring in virgin controls and rats regularly treated with maximum stimulating amounts of growth hormone". As previously noted, the growth-stimulating effect of pregnancy is also attributed to progesterone rather than to pituitary growth hormone.

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[128] Cole and Hart[114] (1938). Bogart, R., *et al.*[127] (1940). Asdell, S. A., *et al.*, Cornell Univ. Agr. Exp. Sta. Memoir 238, 1941.

[129] Stotsenburg, J. M., *Anat. Rec.*, **3,** 233 (1909); **7,** 183 (1913). Van Wagenen, G., *Am. J. Physiol.*, **84,** 461 (1928). Rubinstein[122]. Tang, Y. Z., *Anat. Rec.*, **80,** 137 (1941).

[130] Stotsenburg[129], (1909). Slonaker, J. R., *Am. J. Physiol.*, **93,** 307 (1930); **82,** 318 (1927). Freudenberger, C. B., *et al.*, *Endocr.*, **19,** 347 (1935); *Proc. Soc. Exp. Biol. Med.*, **36,** 144 (1937). Shattock, S. G., and Seligman, C. G., *Proc. Roy. Soc. Med.*, **3,** 102 (1909–10) (Pathol.).

[131] Bogart, R., *et al.*[127] 1940. Asdell, S. A., *et al.*[128] 1941.

[132] Freudenberger[130] 1935 and 1937.

[133] Eckles, C. H., Univ. Missouri Agr. Exp. Sta. Bull. 135, 1915; Eckles, C. H., and Swett, W. W., *Id.*, Res. Bull. 51, 1918.

[134] Mumford, F. B., Univ. Missouri Agr. Exp. Sta. Res. Bull. 45, 1921. McKenzie, F. F., *Id.*, Res. Bull. 118, 1928. Carmichael, W. J., and Rice, J. B., Ill. Agr. Exp. Sta. Bull. 226, 1920.

[135] Briggs, H. M., N. Dak. Agr. Exp. Sta. Bull. 285, 1936.

[136] Bogart, R., *et al.*[127] Cole and Hart[114]. Asdell *et al.*[128], 1941.

[137] Cole and Hart[114].

While ovariectomy tends to stimulate growth (by removing the inhibiting effect of estrogen), orchidectomy (testis removal) tends to depress growth and mature size[138]. Stallions and bulls tend to be larger than geldings and steers. This harmonizes with the previous statement that within limits androgen, but not estrogen, tends to increase growth and mature size. There are some exceptions; when ovariectomized or orchidectomized early enough, man tends to be above normal height because of delay in epiphysial closure.

Farm male animals are castrated in order to reduce restlessness and spontaneous activity[139] (which is, of course, at a feed cost), to facilitate fattening, to increase palatability of the meat, and to increase the dressing percentage.

The data in Tables 7.1 and 7.2 on the growth of normal and castrated lambs[140] and domestic fowl[141] illustrate the situation.

We shall close by considering the question whether or not sex homones can increase reproductive efficiency in good, normal farm animals by speeding up the reproductive process. Theoretically, breeding may begin earlier and animals may be induced to produce larger litters. Actually, the normal breeding age in good, normal animals is probably early enough and the normal litter size is probably large enough for the mother's capacity[142].

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[138] Donaldson, H. H., and Hatai, S., *J. Comp. Neurol.*, **21,** 155 (1911), and many papers. Some of the latest Rubinstein, H. S., *et al.*, *Endocrinology*, **25,** 397 (1939); **28,** 112, 229 (1941). Gordon, M. B., and Fields, E. M., *J. Clin. Endocr.*, **2,** 715 (1942). Dorff, G. B., *J. Clin. Endocr.*, **1,** 940 (1941); *Arch. Ped.*, **59,** 799 (1942).

[139] Hoskins, R. G. [*Am. J. Physiol.*, **72,** 324 (1925)] reported that in female rats gonadectomy decreased voluntary activity up to 90 per cent; Wang, G. [*Comp. psych. mon.* (ser. 2) #6 (1923); *Am. Naturalist*, **58,** 36 (1924)] reported that in male rats gonadectomy decreased voluntary activity up to 60 per cent. However, gonadectomy in rats and dogs decreases the *basal* metabolism, according to Lee, M. O., and Van Buskirk, E. F., [*Am. J. Physiol.*, **84,** 321 (1928)] by only about 10 per cent, which is close to the limit of error in metabolism measurements in rats. Other papers on the influence of sex on spontaneous activity: Slonaker, J. R., *Am. J. Phys.*, **112,** 176 (1935). Richter, C. P., *Comp. Psychol. Monographs*, **1,** 55 (1932); *Quart. Rev. Biol.*, **2,** 307 (1927). Stier, T. J. B., *J. Gen. Psychol.*, **4,** 67 (1930). Bugbee, P., and Simond, A. E., *Endocrinology*, **10,** 349 (1926). There is a large literature on the influence of sex and sex hormones on basal metabolism. Depending on dosage, administration of testosterone may increase metabolism by perhaps 30 per cent in enunchoid individuals [Thompson, W. O., and Heckel, N. J., *J.A.M.A.*, **113,** 2124 (1939); Jones, R., *et al.*, 25th Meeting Assn. Internal Secretion, 1941. Sandiford, I., *et al.*, *J. Clin. Endocr.*, **1,** 931 (1941). See also: Lee, M. O., *Am. J. Phys.*, **86,** 694 (1928) cites a 10 per cent variation in B. M. during estrus cycle. Mitchell, H. H., and Card, L. E., World's Poultry Congress, 1927 (737 Cal/met for capons and 852 for cockerels). Chahovitch, X., *Compt. rend. Soc. Biol.*, 1153 (1928) (castration reduces metabolism to 30-40 per cent). Ritzman, E. G., Colovos, N. F., and Benedict, F., N. H. Agr. Exp. Sta. Tech. Bull. 64, 1936 (5–10 per cent reduction in metabolism of sheep on castration). Shock, N. W., *Am. J. Physiol.*, **139,** 288 (1943) (menarche in girls and metabolism). Korenchevsky, V., British J. Exp. Path. **6,** 21, 158 (1925) (castration affects energy and N metabolism)].

[140] Hunt, W. E., *et al.*, Univ. Md. Agr. Exp. Sta. Bull., 1938.

[141] Waite, R. H., Univ. Md. Agr. Exp Sta. Bull. 235, 1920. For more extensive data on relative growth and feed consumption in roosters, capons and pullets up to 38 weeks, see Annin, G. E., and Halpin, J. G., *Poultry Sci.*, **17,** 419 (1938) (no difference).

[142] Phillips, R. W., *et al.*, *J. Animal Sci.* **1,** 27 (1942).

There is a large literature on superovulation or superfecundity in mammals treated with various gonadotropic preparations[143]. Casida[144] obtained twinning in cattle by injecting F.S.H. preparations followed by artificial insemination, and Loginova[145] induced the production of quintuplet lambs by treating ewes with pregnant-mare serum. Engle[146] obtained up to 29 implanted embryos on the ninth day of pregnancy in mature mice receiving pituitary transplants However, the size of the *delivered* litter was not unusual. Evans demonstrated that superovulation does not increase the number born[147].

TABLE 7.1.—Influence of Castration on Growth, Carcass Weight, and Dressing Percentage of Lambs.

Age (weeks)	Live weight (lbs)		Carcass weight (lbs)		Dressing, per cent	
	Rams	Wethers	Rams	Wethers	Rams	Wethers
5	37.6	34.7	19.4	17.7	51.6	51.0
10	53.0	56.3	25.5	28.0	58.1	49.7
15	57.8	50.8	26.9	23.4	46.5	46.0
20	80.7	77.1	38.5	38.7	47.7	50.2
28	81.3	74.9	37.9	36.9	46.7	49.3
36	95.7	89.5	45.5	44.2	47.6	49.4
44	89.8	90.3	42.9	46.2	47.7	51.1
52	102	101	48.0	50.0	46.9	49.2

TABLE 7.2.—Influence of Castration on Growth and Economy of Gain of White Plymouth Rock Chickens.

(9 weeks of age, 21 cockerels caponized and 21 controls. Growth and feed consumption equal until puberty; after 7 months, capons made more rapid gains.)

Age (weeks)	Weight (lbs)		Feed consumed (lbs)	
	Capons	Cockerels	Capons	Cockerels
9	1.10	1.13		
14	2.23	2.25	4.57	4.75
18	3.19	2.99	6.09	5.83
23	4.71	4.73	6.28	6.23
27	4.86	4.85	7.62	7.00
32	5.77	5.58	8.80	8.68
36	6.24	5.98	9.43	9.41
42	7.13	6.58	9.25	9.47
44	7.42	5.19	5.30	5.19
47	7.76	6.79	5.94	5.39

Cole[143] induced early sex maturation and pregnancy in young rats before normal sexual maturity by injecting pregnant-mare serum. The number of implanted fetuses in these immature rats was up to 28. One rat uterus contained 26 normal fetuses on the seventeenth day of pregnancy; another had 23 living fetuses on the twenty-first day. In some cases 17 living young were born. The young mothers were not injured by the early pregnancies and extraordinarily large litters, but actually increased in body weight and in length beyond the control animals.

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[143] Cole, H. H., *Am. J. Physiol.*, **119**, 704 (1937). Casida, L. E., *et al.*, *Am. J. Vet. Res.*, **4**, 76 (1943).

[144] Casida, L. E., *et al.*, Proc. Am. Soc. Animal Prod., 33 Annual Report, p. 302, 1940.

[145] Loginova, N. V., *et al.*, *Probl. Zivotn.*, **10**, 114 (1938).

[146] Engle, E. T., *Proc. Soc. Exp. Biol. Med.*, **25**, 84 (1927); *Endocrinology*, **15**, 405 (1931).

[147] Evans, H. M., Am. Anat. Soc. Spring Meeting, 1940.

An interesting aspect of Cole's experiments is that the influence of pregnant-mare serum gonadotropic hormones on litter size in rats rapidly decreased with the age of the mother. In mice[147a], on the other hand, superovulation was induced in mature animals with pituitary implants, and in cats[148] by subcutaneous injection of F.S.H. followed by the intravenous injection of L.H.

Research is being conducted on the induction of fecundation in seasonal breeders, especially sheep, during the non-breeding season[149]. Estrogen administration (stilbestrol and pregnant-mare serum) led to off-season estrus and ovulation but not to fecundation in sheep[150]. Adjusting the light-to-dark ratio to simulate the natural-breeding season seems promising in view of the results reported by Bissonnette on goats and other species (Ch. 8). Thyroid administration is said to be promising in inducing breeding during the non-breeding season[151].

Minor applications are under investigation, such as the treatment of recurrent or threatened abortion with progesterone[152].

Summarizing, this section (7.2) outlines the role of sex hormones in reproduction, efficiency of agricultural processes, evolution, growth and development and life in general. The reproductive process, however, is not dependent on sex hormones alone but on all hormones acting in harmony, as well as on diet, and on season. This section is, therefore, incomplete by itself; it must be considered in conjunction with all the other sections in this chapter as well as with chapters 6 and 20 (nutrition) and 8 (seasonal effects).

The endocrinology of reproduction illustrates a frequently encountered pattern of endocrine action. The reproductive process is under the control of the gonads (ovaries and testes), and the gonads are under the control of the anterior lobe of the pituitary. In addition, other endocrines, for example, the thyroid and the adrenal cortex, participate in the reproductive and lactation processes. The gonadotropins and sex hormones are produced by the pituitary and by the gonads respectively; but gonadotropins are also produced by the placenta and perhaps other tissues, and sex hormones may also be produced by the adrenal cortex (Sect. 7.4). The gonadotropins are usually excreted with the urine; but in gestating horses the blood is very rich in gonadotropins[153]. Yet, unlike gonadotropin in women, it is not excreted in the urine, perhaps because, unlike other gonadotropins, the mare's placental gonadotropins are more complicated, and are apparently in peptide form[154]. The sex hormones are thought to be excreted in the urine; but stallions and bulls excrete mostly female, not male, sex hormones; perhaps the hormones in the urine are not the original sex hormones. There are evidently species, sex, and age differences. There are rules and rule exceptions. The mare blood-serum gonadotropin is apparently very potent; its intravenous injection in 36 women on varying days of the menstrual cycle induced ovulation[155].

[147a] Smith, P. E., and Engle, E. T., *Am. J. Anat.*, **40**, 159 (1927). Engle, E. T., *Proc. Soc. Exp. Biol. Med.*, **25**, 84 (1927); *Endocrinology*, **15**, 405 (1931).

[148] Foster, M. A., and Hisaw, F. L., *Anat. Rec.*, **62**, 75 (1935).

[149] Hammond, J. Jr., Hammond, J. and Parkes, A. S., *J. Agr Sci.*, **32**, 308 (1942). Warwick, E. J., and Casida, L. E., *Endocrinology*, **33**, 169 (1943).

[150] Frank, A. H., and Appleby, A. J., *Animal Sci.*, **2**, 251 (1943).

[151] Turner, C. W., unpublished observations.

[152] Katz, J., *et al.*, *J. Clin. Endocr.*, **1**, 838 (1941).

7.3: Energy-metabolism hormones, thyroid and adrenal-medulla. All hormones are energy-metabolism catalysts. This section is concerned with the best-known energy-metabolism endocrine, the thyroid, with brief notes on the adrenal-medulla, and on their interrelations with other endocrines and with the nervous system.

As might be expected, there is a large literature on the thyroid, its anatomy[156], evolution[157], chemistry[158], pathology[156,159], and so on.

7.3.1: The thyroid in growth, development, milk production, and egg production. Modern thyroid research, that is, one involving thyroid removal and replacement therapy, began over half a century ago[160]. It is now generally known that myxedema is associated with thyroid loss or deficiency in the adult and cretinism with thyroid absence or deficiency from early life. On administration of thyroactive material, developmental normality may be resumed under certain conditions.

This situation is demonstrated by surgical removal of the thyroid in infant animals and noting the course of growth and development of the animal with and without thyroactive medication. Fig. 7.5 represents a recent attempt to produce cretin cattle[161] by surgical removal of the thyroid (thyroidectomy at 50 days of age). The mature body weight is seen, in Fig. 7.5, to be half normal and the energy metabolism per unit urea 40 per cent below the normal control.

Similar results are available on rabbits, goats, sheep[162], mice[163], guinea pigs[164], cats[165], rats[166], monkeys[167], dogs[168], chickens[169], and other species[170].

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[153] Cole, H. H., and Hart, G. H., *Am. J. Physiol.*, **93**, 57 (1930).

[154] Cartland, G. F., and Nelson, J. W., *J. Biol. Chem.*, **119**, 59 (1937).

[155] Davis, M. E., and Koff, A. K., *J. Obst. Gyn.*, **36**, 183 (1938).

[156] See, for example, Sloan, E. P., "The thyroid; surgery; syndrous; treatment," C. C. Thomas, 1936.

[157] Little, M. E., "Structure of the vertebrates," Farrar and Rinehart, 1937.

[158] Harrington, C. R., "The thyroid gland, its chemistry and physiology," Oxford Univ Press, 1933.

[159] Means, J. H., "The thyroid and its diseases", Lippincott, 1937.

[160] Schiff, M., *Rev. Med. de la Suisse*, **4**, 65 (1884).

[161] Brody, S., and Frankenbach, R. F., Univ. Missouri Agr. Exp. Sta. Res. Bull. 349, 1942.

[162] From the literature: Rabbit data, Basinger, H. R., "Control of cretinism," Univ. Chicago dissertation (no date on author's copy); sheep and goats, **Todd, T. W., and**

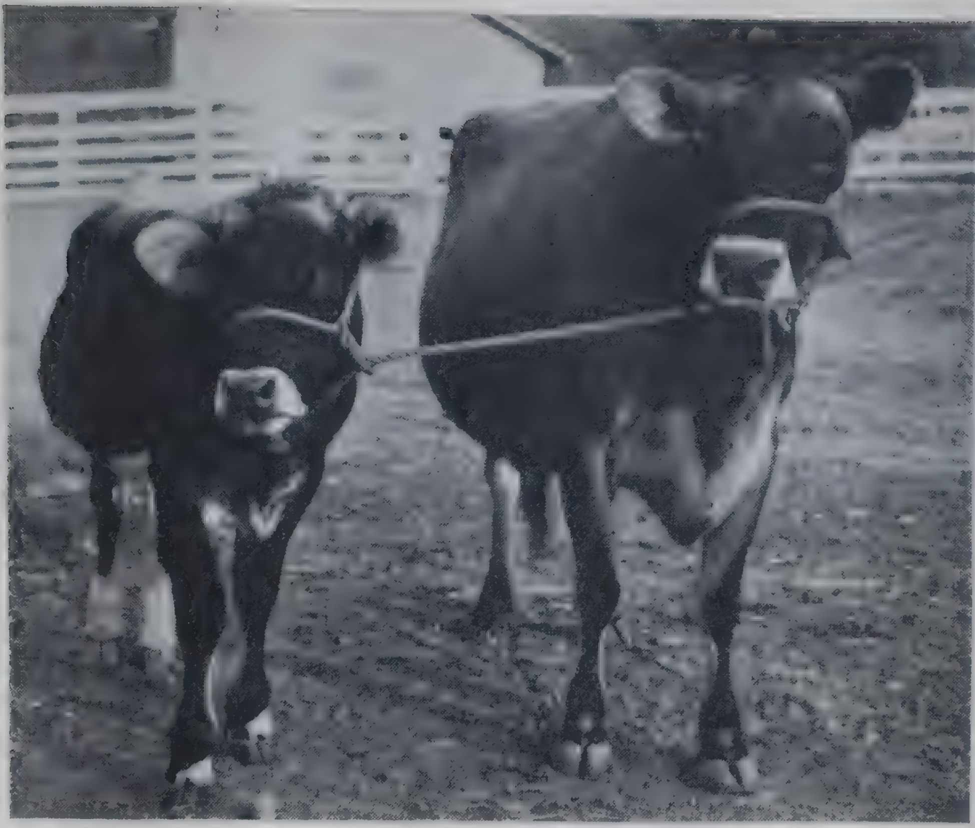

Fig. 7.5a—Comparison of thyroidectomized and normal Jersey cattle at the same age.

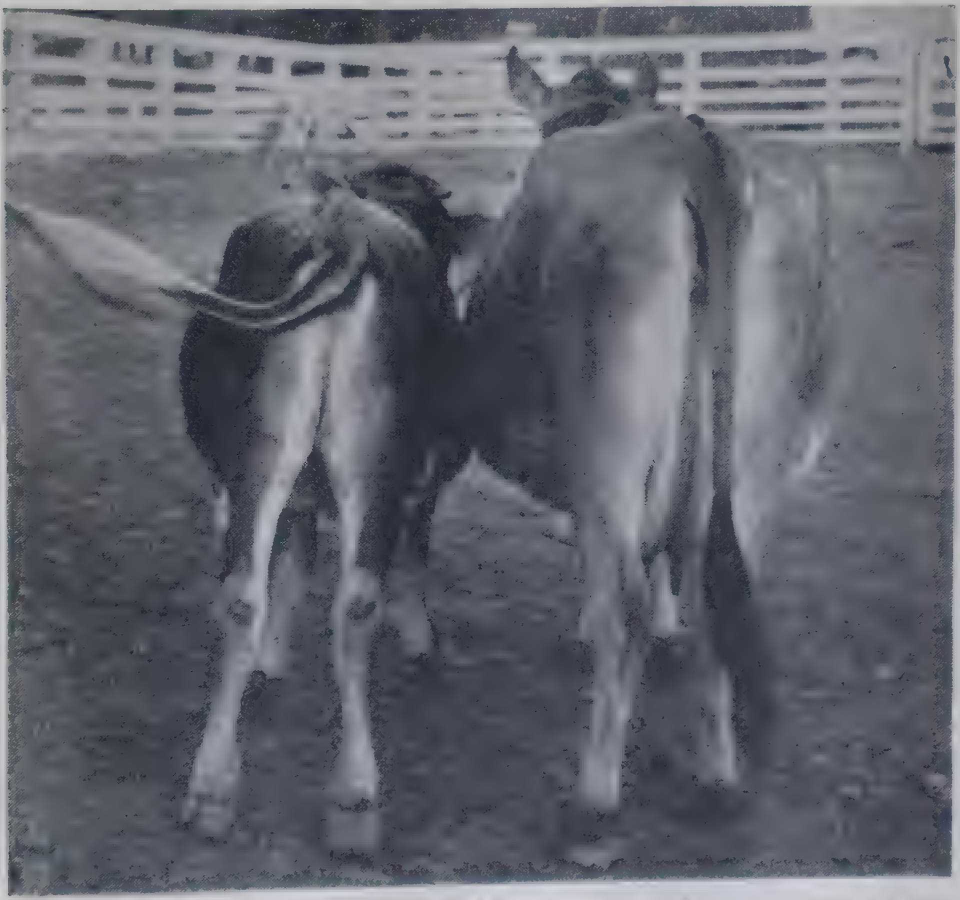

Fig. 7.5b—Comparison of thyroidectomized and normal Jersey cattle at the same age.

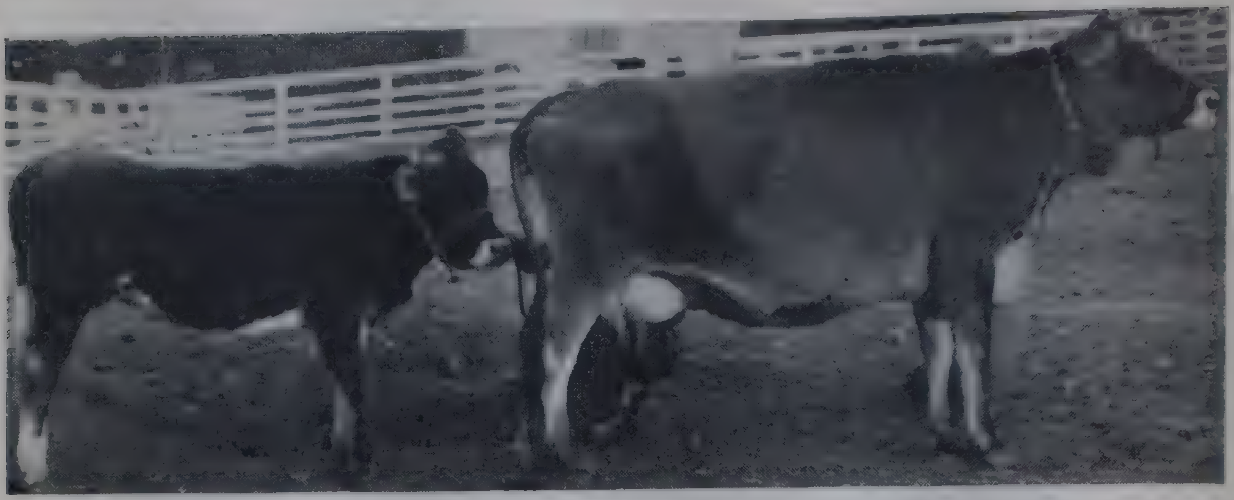

Fig. 7.5c—Comparison of thyroidectomized and normal Jersey cattle at the same age.

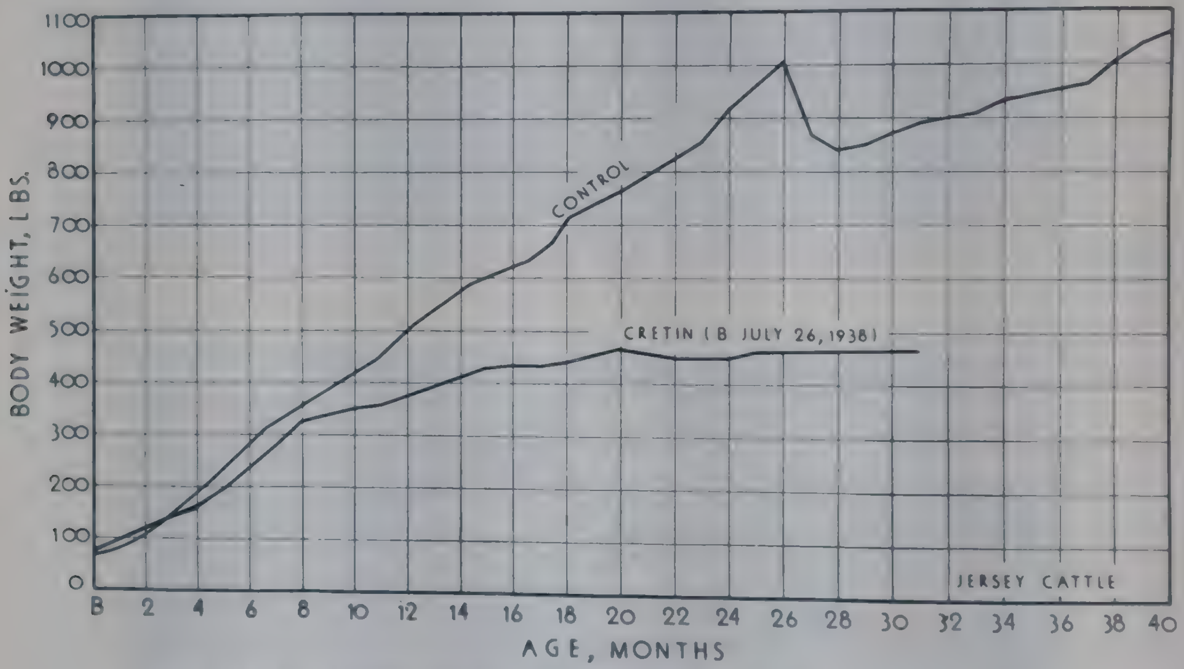

Fig. 7.5d—Comparison of growth curves of the same animals.

The thyroid is indispensable for amphibian metamorphosis. Thyroidectomized tadpoles grow in size but do not metamorphose into frogs[171]. On

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W. W., and Wharton, R. E., *Am. J. Anat.*, **63,** 37 (1938). Simpson, S., "Thyroidectomy in sheep and goats," *Quart. J. Exp. Physiol.*, **6,** 119 (1913); **14,** 161, 185 (1924); *Am. J. Physiol.*, **80,** 735 (1927). Simpson, E. D., *Proc. Soc. Exp. Biol. Med.*, **24,** 289 (1927).

[163] Davenport, C. B., and Swingle, W. W., *J. Exp. Zool.*, **48,** 395 (1927).

[164] Silberberg, M. and R., *Am. J. Path.*, **16,** 505 (1940). Williams, C., Phelps, D., and Burch, J. C., *Endocrinology*, **29,** 373 (1941).

[165] Dott, N. M., *Quart. J. Exp. Physiol.*, **13,** 241 (1923).

[166] Kojimi, M., *Quart. J. Exp. Physiol.*, **11,** 351 (1917). Hammett, F. S., *Quart. Rev. Biol.*, **4,** 353 (1929). Laqueur, E., *et al.*, *Acta brevia Neerl*, **11,** 46 (1941). Fishbourne, M., *Endocrinology*, **22,** 122 (1938).

[167] Fleishchmann, W., *et al.*, *Endocrinology*, **32,** 238 (1943).

[168] **Binswanger, F.,** *Endocrinologie*, **17,** 150 (1936).

[169] **Landauer, W.,** *Am. J. Anat.*, **43,** 1 (1929).

[170] Salmon, T. N., *Endocrinology*, **23,** 446 (1938). Hunter, M. W., and Sawin, P. B., *Am. J. Anat.*, **71,** 417 (1942).

[171] Allen, B. M., *Science*, **44,** 755 (1916); Hoskins, E. R., and M. M., *Anat. Rec.*, **24,** 395 (1917).

the other hand, feeding thyroid to small tadpoles metamorphoses them into pigmy froglets[172]. Indeed, one assay method for thyroid activity is to determine the dosage for transforming a tadpole into a frog[173]. The Mexican aquatic lizard *axolotl* normally spends its life in this ("tadpole" or larval) form. On feeding thyroid it is changed to the terrestial (lung-breathing) salamander (uradele) *ambystoma*, and this metamorphosis is likewise used as assay for thyroxine hormone[174]. It is evident that the thyroid has developmental and differentiating factors as well as growth functions.

Cretin animals have a typical appearance: short legs, short dished (bulldog) face, rough dry skin and hair, "pot-belly", and so on. Sheep thyroidectomized between one and five months developed some characteristics of primitive sheep. The long bones and epiphyses fail to grow out. The effect of thyroid removal depends on the age at which it is performed. In our experience[161] the earlier the age of thyroidectomy the more severe the results[175], although Hammett[176] reported the opposite.

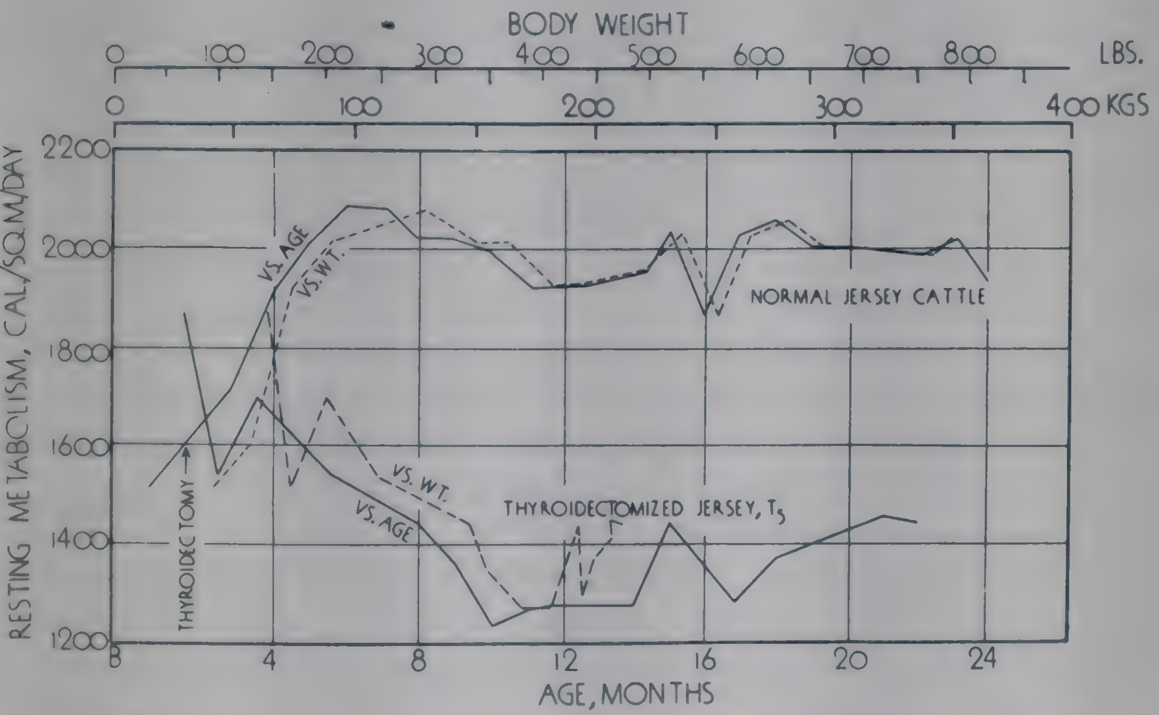

Fig. 7.5e—Comparison of resting heat production of the same cattle.

About 1895 Magnus-Levy[177] discovered that loss of the thyroid may reduce the basal energy metabolism by nearly half, and that suitable thyroid feeding may almost double the metabolism. Metabolic rate was, therefore, generally adopted as a measure of thyroid function. More recently, thiourea and related anti-thyroid compounds have been investigated as assay agents[178].

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[172] Gudernatsch, *Am. J. Anat.*, **15**, 431 (1913-14); *Arch. Entw. Mech. Org.*, **40**, 571 (1914); **41**, 57 (1915). Uhlenhuth, J. F., *J. Gen. Physiol.*, **1**, 473 (1919).

[173] Cuyler, W. K., Stimmel, B. F., and McCullagh, D. R., *J. Pharmak. Exper. Therap.*, **58**, 286 (1936).

[174] Spaul, E. A., *Brit. J. Exp. Biol.*, **2**, 1 (1924).

[175] *Cf.* Simpson, S., *Quart. J. Exp. Physiol.*, **6**, 119 (1913); **14**, 161 (1924). Salmon[170] (1938); *Endocrinology*, **29**, 291 (1941). Straus, W. L., *Endocrinology*, **32**, 238 (1943).

[176] Hammett, F. S., *Am. J. Physiol.*, **68**, 1 (1924); **76**, 69 (1926).

[177] Magnus Levy, A., *Berlin. Klin. Wochensch.*, **32**, 650 (1895); *Deut. Med. Woch.*, **22**, 491 (1896); *Z. Klin. Med.*, **33**, 269 (1897). For review of the literature, see the latest edition of Du Bois, E. F., "Basal metabolism in health and disease."

The acceleration of bodily oxidation is, however, only one of the thyroid's catalytic manifestations. Dinitrophenol may be used to raise to normal the energy metabolism of a thyroidectomized animal but not the growth or development rate. In fact, all anabolic processes are retarded by thyroidectomy, including the rates of digestion[179], peristalsis[180], assimilation, especially of carbohydrates[181] (perhaps associated with decreased phosphorylation), circulation rate[182], milk production[183], egg production[184], muscular activity[185], nervous irritability[186], and so on. There is a possibility that the thyroid elaborates more than one active principle, perhaps one which accelerates the pulse rate independently of increased metabolism[187].

Hypothyroidism is associated with a tendency to fattening. This suggested the investigation of the influence of partial thyroidectomy, surgical or perhaps by anti-thyroid drugs (as thiourea) administration, on the fattening of farm animals. Partial surgical thyroidectomy is said to yield desirable results in fattening steers[188], and also pigs[189] thyroidectomized when weighing 30 to 40 kg, but not at later ages. Zorn[189] concluded that the feed utilization was shifted to a lower efficiency level, from muscle and skeletal growth to fattening. (It requires more dietary energy to produce a calorie of fat than of carbohydrate; the exact cost depends on the nature of the diet, age, and other conditions.) The term "fattening" under these conditions is ambiguous unless accompanied by data on the composition of the gains[190].

It is human to assume, as did Moussu[191] in 1899, that if some thyroid is essential for normal growth, a little more thyroid would result in supernormal growth, and he indeed reported acceleration of the growth rates in normal dogs by feeding small amounts of thyroid tissue. The growth, however, stopped earlier than in the controls, and mature size was slightly subnormal. This 1899 result on dogs was confirmed in 1923 by Dott[192]. Thyroid medication accelerated growth, and was followed by premature cessation of growth with ultimate somewhat subnormal size. A considerable literature has developed since Moussu's report.

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[178] Dempsey, E. W., and Astwood, E. B., *Endocrinology*, **32**, 455 (1943). Turner, C. W. and Reineke, E. P., unpublished data.

[179] Eidinova, M., *Bull. biol. Med. Exptl. U.S.S.R.*, **1**, 316 (1936).

[180] Althausen, T. L., *Tr. Am. Soc. Study Goiter*, (1939) p. 37. Castleton, K. B., and Alvarez, W. C., *Am. J. Dig. Dis.*, **8**, 473 (1941). Morrison, S., and Feldman, M., *Id.*, **6**, 549 (1939).

[181] Althausen, T. L., and Stockholm, M., *Am. J. Physiol.*, **123**, 577 (1938).

[182] Abramson, D. L., and Sidney, M. F., *Arch. Int. Med.*, **69**, 409 (1942).

[183] Graham, W. R., Jr., *J. Nut.*, **7**, 407 (1934).

[184] Winchester, C. F., *Endocrinology*, **24**, 697 (1939); Missouri Agr. Exp. Sta. Res. Bull. 315, 1940. Taylor, L. W., and Burmester, B. R., *Poultry Sci.*, **19**, 326 (1940).

[185] Hall, V. E., and Lindsay, M., *Endocrinology*, **22**, 66 (1938). Lee, M. O., and Van Buskirk, E. F., *Am. J. Physiol.*, **84**, 321 (1928).

[186] Brody, E. B., "The thyroid and variability of muscular activity in the rat," *Endocrinology*, **29**, 916 (1941); *J. Comp. Psychol.*, **34**, 213 (1942).

[187] Meyer, A. E., *Endocrinology*, **24**, 806 (1939); **27**, 97 (1940); **28**, 816 (1941).

[188] Andrews, F. N., and Bullard, J. F., *Proc. Am. Soc. Animal Production*, (1940), p. 112; *J. Am. Vet. M. Assn.*, **102**, 376 (1943).

[189] Zorn, W., *Zuchtungskunde*, **14**, 376 (1939).

[190] *Cf.* Simpson, E. D., *Proc. Soc. Exp. Biol. Med.*, **24**, 289 (1927).

[191] Moussu, M. G., *Compt. rend. soc. biol.*, **51**, 241 (1899).

Much of this literature[193] on the influence of thyroid administration on growth is conflicting because of the variability of the thyroid effect with species, age, sex, external temperature and particularly dosage. There is one physiologically optimal thyroid-dosage level. Below this level the results are not impressive because the animal's thyroid probably reduces its own hormone production in proportion to the amount of thyroid administered (in accordance with the principle of homeostasis, Ch. 10). Above the optimal level, the catabolic effect of the thyroid hormone overbalances the anabolic effect; indeed, the extra hormone often becomes toxic.

This optimal thyroid dosage, moreover, varies with the external temperature[194] (Ch. 11) and with the species. Thyroid administration increases heat production; therefore, animals having a good heat-dissipating mechanism would naturally be expected to do better under thyroid treatment than species not so well equipped for heat dissipation.

Then, too, thyroid administration increases the neuro-muscular irritability in particular and variability in general[186]. This is not unexpected, since thyroid accelerates the metabolism of nerve tissue[195] and affects corresponding neuromuscular activity[196], cortical alpha rhythms[197], thresholds to light and sound[198], and so on. This exaggerated variability of hyperthyroid animals complicates the interpretation of the results of thyroid-hormone administration.

There is a particularly striking species variability in the reaction to thyroid administration. Thus the growth rate of mice is increased by a certain thyroid dosage. This was observed by Robertson[199] (who fed the equivalent of 19 mg fresh thyroid per animal per day), and recently confirmed[200], by daily injection of 0.01 to 0.03 mg crystalline thyroxine). The mature size was not changed; only the maturation rate or early growth rate was accelerated. Thyroid administration to young mice and dogs accelerates the growth of the epiphysial cartilage and thus leads to premature epiphysiodiaphysial union[200].

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[192] Dott, N. M., *Quart. J. Exp. Physiol.*, **13**, 122 (1923).

[193] For perhaps the best general review on the effects of feeding thyroid on growth and related substances, see Schneider, B. A., *Quart. Rev. Biol.*, **14**, 289 (1939). As it relates to humans, see Lerman, Jacob, *J.A.M.A.*, **117**, 349 (1941). For a late review, see Koger, Marvin, and Turner, C. W., "The effect of mild hyperthyroidism on growing animals", University of Missouri Agr. Exp. Sta. Res. Bull. 377, 1943. See also Silberberg, M. and R., *Arch. Path.*, **36**, 512 (1943).

[194] Dempsey, E. W., and Astwood, E. B., *Endocrinology*, **32**, 455 (1943). (Thyroxine secretion is increased by cold and reduced by heat. A new method is described for thyroxin assay by the extent of thyroid hypertrophy associated with thiouracil administration.)

[195] Cohen, R. A., and Gerard, R. W., *J. Cell. Comp. Physiol.*, **10**, 223 (1937). Rossiter, R. J., *J. Clin. Endoc.*, **2**, 165 (1940). MacLeod, L. D., and Reiss, M., *Biochem. J.*, **34**, 820 (1940). Gellhorn, E., and Feldman, J., *Endocrinology*, **29**, 467 (1941).

[196] Hall, V., and Lindsay, M., *Endocrinology*, **22**, 66 (1939).

[197] Ross, D., and Schwab, R., *Id.*, **25**, 75 (1938).

[198] Asher, L., *Ohio J. Sci.*, **37**, 379 (1937).

[199] Robertson, T. B., *Austr. J. Exp. Biol. Med.*, **5**, 69 (1928).

[200] Koger and Turner[193].

Rats might be expected to react to thyroxine as do mice. But Koger and Turner[199] could not accelerate the growth of rats, guinea pigs, or rabbits by any thyroid dosage. There is evidently a species difference. Moreover, different strains of rats reacted differently to a given thyroid dosage and females appeared to tolerate the hormone better than males[202]. The growth rate of the smaller breeds of domestic fowl is apparently accelerated by thyroid administration, but not of the larger[203].

The growth of some children is accelerated by feeding about 1 grain (65 mg) of desiccated thyroid per day. This favorable response of *some* children was explained by one author as due to a "masked hypothyroidism"[204]. The results are suggestive, but the individual variations in response cast doubt on its significance for the practical acceleration of the growth process.

A noteworthy observation by Koger and Turner[199] is that the total energy stored was the same in the growth-accelerated and control mice, the difference in size being due solely to differences in the storage of water, protein, and fat. The thyroid-dosed mice had a higher water and nitrogen and a lower fat content.

The other thyroid-feeding effect, long known, is hypertrophy of the heart, liver, spleen, and adrenals[205]. The pancreas tends to hypertrophy and the insulin content is increased[206]. Of course, the thyroid gland is depressed[207] (Sect. 7.1) in accordance with the principle of homeostasis (Ch. 10) and so is the pituitary[208].

As regards the influence of thyroid on other productive processes, it is generally known that thyroid medication is useful in some cases of human sterility[209]. It may be similarly useful in farm-animal sterility, especially with the loss of fertility during aging[210].

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[200] Falkenheim, M., *Am. J. Physiol.*, **138**, 175 (1943). Dott, N. M.[188]

[201] Gudernatsch, J. F., *Am. J. Physiol.*, **36**, 370 (1915) reported that thyroid feeding depressed growth in rats.

[202] Turner, C. W., unpublished data.

[204] Tepper, A., and Cohen, P., *Am. J. Dis. Child.*, **35**, 205 (1938). Dorff, G. B., "Masked hypothyroidism," *J. Pediat.*, **6**, 788 (1935). Molitch, M., *Endocrinology*, **22**, 422 (1938). Wilkins, L., *J. Am. Med. Assn.*, **114**, 2382 (1940); **116**, 2459 (1941). Lerman, J., *J. A. M. A.*, **117**, 349 (1941). Thyroxine administration increased the growth rate and heat production of dwarf mice, but so did a higher environmental temperature, indicating a non specific effect (Boettiger, E. G., *Endocrinology*, **28**, 785 (1941)). Hertz, S., and Galli Mainini, C., *J. Clin. Endocr.*, **1**, 518 (1941).

[205] The literature on the effect of thyroid administration on organ size is very large. See among others, Hoskins, E. R., *J. Exp. Zool.*, **21**, 295 (1916). Hammett, F. S., *Am. J. Physiol.*, **76**, 69 (1926); *Am. J. Anat.*, **39**, 219 (1927). Korenchevsky, *et al.*,[152] (1943).

[206] Fraenkel-Conrat, H., *et al.*, *Endocrinology*, **30**, 485 (1942). Kojima, M., *Quart. J. Exp. Physiol.*, **11**, 351 (1917). Reforzo Membrives, J., *Endocrinology*, **32**, 262 (1943).

[207] Reforzo Membrives[206] (1943). Cameron, A. T., and Carmichael, J., *J. Biol. Chem.*, **46**, 35 (1921). Korenchevsky[152] (1943).

[208] Herring, P. T., *Quart. J. Exp. Physiol.*, **11**, 231 (1917). Evans, H. M., and Simpson, M. E., *Anat. Rec.*, **45**, 215 (1930). Campbell, M., and Wolfe, J. M., *Proc. Soc. Exp. Biol. Med.*, **32**, 205 (1934).

Crew[211], indeed, published spectacular observations on "rejuvenation of the aged fowl through thyroid medication". He used 5 cocks and 7 hens, 5 to 8 years of age, "all showing the classical signs of old age". The medication consisted in feeding desiccated thyroid equivalent to 0.2 mg iodine per day during the first fortnight, 0.4 mg iodine per day the second fortnight, and 0.8 mg iodine per day thereafter ("no control pan was maintained", a rather serious methodologic deficiency). The hens "quickly started to produce eggs at a faster rate . . . head furnishings became red and turgid, the plumage tight and close . . . all the birds became rejuvenated, looking fresh and being active . . . none of the hens became broody during the course of the experiment (12 months), though six out of the seven belonged to the setting breeds". Three months after cessation of the thyroid feeding "they became progressively senile", two dying from roup and pneumonia, two from peritonitis associated with oviduct rupture, one "died of what must be diagnosed as old age, no organic lesion was present . . . all the hens that are still active exhibit the classical signs of ovarian atrophy". It is strange that no one followed up this work in spite of the universal interest in rejuvenation and the extremely important agricultural implications of this observation.

Preliminary observations[212] on two-year old Leghorn hens indicate greatly increased egg production over several months associated with feeding thyroactive material at a certain level. It is, of course, known that the thyroid is involved in egg production, and that thyroidectomy in mature fowls severely reduces egg production[213] which may be restored by suitable thyroid feeding.

There is also considerable literature[214] indicating that milk production in dairy cattle may be increased up to 20 per cent and fat production up to 50

[209] See among others, Du Bois, E. F., "Metabolism in Health and Disease," Lippincott, several editions. Means, J. H., "The Thyroid and Its Diseases," Lippincott, 1937. Foster, F. C., and Thornton, M. J., *Endocrinology*, **24**, 383 (1939). King, E. L., and Herring, J. S., *J. A. M. A.*, **113**, 1300 (1939). Davis, C. H., *Am. J. Obst.*, **46**, 85 (1943). Hamblen, E. C., *et al.*, *J. Clin. Endocr.*, **1**, 523 (1941). Drill, V. A., *et al.*, *Endoc.*, **32**, 327 (1943). Parkin, G., and Greene, J. A., *J. Clin. Endocr.*, **3**, 466 (1943).

[210] Reineke, E. P., and Turner, C. W., *J. Am. Vet. Med. Assn.*, **102**, 105 (1943). *J. Clin. Endocr.*, **3**, 1 (1943).

[211] Crew, F. A. E., *Proc. Roy. Soc. Edinburgh*, **45**, 252 (1924). Also, Cole, L. J., and Hutt, F. B., *Poult. Sci.*, **17**, 60 (1928).

[212] Turner, C. W., *et al.*, unpublished data, Dairy Dept., University of Missouri, July 1943.

[213] Winchester, C. F., *Endocrinology*, **24**, 697 (1939); Univ. Missouri Agr. Exp. Sta. Res. Bull 315, 1940.

[214] Graham, W. R., Jr., and *Biochem. J.*, **28**, 1968 (1934). Herman, H. A., Graham, W. R., Jr., Turner, C. W., Ralston, N. P., Cowsert, W. C., and Ragsdale, A. C., Missouri Agr. Exp. Sta. Res. Bulls. 275, 1938, and 317, 1940. See also, Jack, E. J., and Bechdel, S. I., *J. Dairy Sci.*, **18**, 195 (1935). Folley, S. J., and White, P., "Thyroxine on milk secretion and on the phosphatase of the blood and milk," *Proc. Roy. Soc.*, **120B**, 346 (1936). Smith, J. A. B., and Dastur, N. N., "Thyroxine and blood lipoids and milk fat," *Biochem. J.*, **34**, 1093 (1940).

per cent, at least for short periods on the declining segment of the lactation curve, by feeding thyroactive material (15 gm iodinated casein daily). However, the ascorbic acid content (no data on other vitamins) in the milk is reduced[215].

From the homeostatic viewpoint (Ch. 10) one would infer that it is not safe to meddle with a naturally evolved physiological system by upsetting the normal balance, as is done by thyroid or other drug administration. Thus long-continued thyroid administration tends to lead to thyroid atrophy, adrenal hypertrophy[216], damage of the circulatory-renal[217] and hepatic[218] systems, and accelerate the rate of senescence[219]. But, as above noted, such injuries, even if present, may be without agricultural significance when, for example, thyroid is fed to three year-old hens the last year before slaughter.

Inexpensive iodinated casein[220] and iodinated peanut protein[221] preparations are available, as well as crystalline-*d-l*-thyroxine[222] and also *l*-thyroxine[223], which may be used conveniently for experimental and feeding purposes.[224]

It appears that Morse[225], in 1914, demonstrated that protein treated with iodine exerts thyroxine effects. Subsequently, several investigators[226] demonstrated the presence of thyroxine in casein and other protein treated with iodine.

It should be noted, in conclusion, that, as might be expected, thyrotropic hormone exerts effects (by way of thyroid) similar to thyroxine; thus there appears to be a correlation between thyrotropic hormone concentration (in the anterior pituitary) and the growth rate[227].

7.3.2: Other thyroid interrelations. The preceding section was concerned with the influence of thyroidectomy and thyroid medication on agriculturally productive processes, growth and development, egg production, and milk production. This section is concerned with other thyroid interrelations, particularly those with diet and with other hormones.

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[215] Van Landingham, A. H., Henderson, H. O., and Weakley, C. E. Jr. Abstracts, Meeting Am. Chem. Soc., Sept. 9, 1943, p. 10B.

[216] Reforzo-Membrives[206] (1943). Hoskins, R. G., *J.A.M.A.*, **55**, 1724 (1910); *Am. J. Physiol.*, **26**, 426 (1910).

[217] McEachern, D., and Rake, D., *Johns Hopkins Hosp. Bull.*, **48**, 273 (1931); Goodall, J. S., and Rogers, L., *Lancet*, **1**, 486 (1927); Goodpasture, E. W., *J. Exp. Med.*, **34**, 407 (1921). Menne, F. R., *et al.*, *Arch. Path.*, **17**, 333 (1934). Hashinoto, H., *Endocrinology*, **5**, 579 (1921). Rake, G., and McEachern, D., *J. Exp. Med.*, **54**, 23 (1931). Schultz, M. P., Public Health Repts., July 7, 1939 (p. 1205). Bodansky, M., *et al.*, *Proc. Soc. Exp. Biol. Med.*, **32**, 597 (1935). Andrus, E. C., and McEachern, D., *Am. J. Med. Sci.*, **183**, 741 (1932).

[218] Drill, V. A., *et al.*, *Am. J. Physiol.*, **136**, 762 (1942); **138**, 370 (1943).

[219] Silberberg, M. and R., *Arch. Path.*, **36**, 512 (1943).

[220] Reineke, E. P., and Turner, C. W., Univ. Missouri Agr. Exp. Sta. Res. Bull. 355, 1942 (full history and bibliography). Reineke, Williamson, M. B., and Turner, *J. Biol. Chem.*, **147**, 115 (1943); *J. Clin. Endocr.*, **3**, 1 (1943).

[221] Blaxter, K. L., *Nature*, **152**, 751 (1943).

[222] Reineke and Turner, *J. Biol. Chem.*, **149**, 555 (1943).

[223] Reineke and Turner, *Id.*, **149**, 563 (1943).

[224] Reineke and Turner, *J. Dairy Sci.*, **25**, 393 (1942).

[225] Morse, M., *J. Biol. Chem.*, **19**, 421 (1914).

[226] See, for example, Harrington, C. R., and Pitt Rivers, R. V., Nature, **144**, 205 (1939). Ed. in *J.A.M.A.*, **115**, 46 (1940). Reineke and Turner.[222-224]

[227] Turner, C. W., and Cupps, V. T., *Endocrinology*, **24**, 650 (1939); **26**, 1042 (1940). Elijah, H. D., and Turner, C. W., Univ. Mo. Agr. Exp. Sta. Res. Bull. 357, 1942.

A. Thyroid and nutrition. Thyroid administration, or hyperthyroidism, accelerates all metabolic processes. Hyperthyroidism is consequently associated with a correspondingly increased need for all nutrients—proteins, minerals, and vitamins. If the calorie and protein needs are satisfied but the vitamin needs are not, hyperthyroidism obviously will be associated with and show symptoms of hypovitaminosis. Such cases have been definitely reported for thiamine[228, 229] and less definitely for pyridoxine and pantothenic acid[229]. The cardiac symptoms[230] (bradycardia and tachycardia) and hepatic damage (particularly low liver glycogen[231]) associated with hyperthyroidism are confused by the cardiac and hepatic syndrom associated with insufficiency of the B vitamins, particularly of thiamine.

While there is a large literature[232] indicating some "antagonism" between thyroxine and the B vitamins, this may be true only in the sense that thyroxine accelerates all metabolic processes, with a consequent increase in need of the vitamins. Hypovitaminosis effects are probably secondary to primary hyperthyroidism.

Hyperthyroidism increases the requirements for vitamin A, as for other vitamins. But there are, in addition, other interrelations between vitamin A and thyroxine. One of these is that vitamin A deficiency leads to thyroid hypertrophy and degeneration of the epithelial cells[233]. This, however, is not an exclusive property of vitamin A. A second, more characteristic, effect is that vitamin A (fish liver oil) excess depresses not only thyroid activity but apparently the effect of thyroxine as well. As little as 1 per cent cod liver oil in the stock diet of rats during 4 months reduced the thyroid weight[234].

The body weight loss associated with thyroid administration may be reduced or prevented by sufficient vitamin A administration[235]. It has long been known that excess vitamin A delays metamorphosis in amphibians[236],

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[228] Sure, B., and Buchanan, K. S., *J. Nut.*, **13,** 513 (1937). Drill, V. A., and Sherwood, C. R., *Am. J. Physiol.*, **124,** 683 (1938). Williams, R. H., *et al.*, *Arch. Int. Med.*, **72,** 353 (1943).

[229] Drill, V. A., *et al.*, *Am. J. Physiol.*, **132,** 629 (1941); **135,** 474; **136,** 762 (1942); *Endocr.*, **31,** 245, 567 (1942); **32,** 327 (1943).

[230] Drill, *et al.*, *Am. J. Physiol.*, **138,** 370 (1943).

[231] Drill, *J. Nut.*, **14,** 355 (1937). McIver, M. A., and Winter, E. A., *J. Clin. Inv.*, **21,** 191 (1942).

[232] Korenchevsky, V., *et al.*, *Brit. Med. J.*, **1,** 245 (1943). Drill, V. A., *Physiol. Rev.*, **23,** 355 (1943).

[233] McCarrison, R., *Brit. Med. J.*, **1,** 989 (1931). Coplan, H. M., and Sampson, M. M., *J. Nut.*, **9,** 469 (1935). Sure, B., *Endocr.*, **23,** 575 (1938).

[234] Freudenberger, C. B., and Clausen, F. W., *J. Nut.*, **10,** 549 (1935).

[235] Drill[229] and *Proc. Soc. Exp. Biol. Med.*, **39,** 313 (1938). Logras, G., and Drummond, J. C., *Biochem. J.*, **32,** 964 (1938).

[236] McCarrison, R., *Ind. J. Med. Res.*, **11,** 1 (1923).

and it was observed more recently that vitamin A administration partially counteracts the acceleration of energy metabolism following thyroid feeding[237].

A third interrelation between vitamin A and the thyroid is that carotene cannot be converted to vitamin A in the absence of the thyroid. Hence, the prevalence of xerophthalmia in thyroidectomized animals, such as rabbits[238], which normally obtain their vitamin A from carotene. The yellow color of milk produced by thyroidectomized goats that normally produce a white milk[239] is similarly explained.

The above results indicate that high intake of fish-liver oil should be very helpful in hyperthyroid- and Graves'-disease conditions; and that hypothyroid individuals should receive vitamin A as such, and not as carotene. Hyperthyroidism increases the need for ascorbic acid as it does for the A and B vitamins, and ascorbic acid deficiency in guinea pigs leads to hemorrhagic infiltration and hyperplasia of the thyroid gland.

High ascorbic acid dosage appears to decrease the energy metabolism in hyperthyroidism[240]. Hyperthyroid individuals should, therefore, benefit by high ascorbic acid intake, as by high vitamins A and B intake.

While little is known about the interrelation between vitamin D and thyroid function, it is definitely known that hyperthyroidism greatly accelerates calcium catabolism[241], perhaps in proportion to the increase in energy in protein catabolism[242], which may reach 100 per cent above the normal level.

The foregoing discussion indicates how dietary factors may exert hormone or anti-hormone effects because of their interrelations with endocrines or the hormones. There are many such interrelations, such as those between vitamin E and the pituitary (Chs. 6 and 20). The "pituitary-like effects of yeast extracts"[243] may be explained by similar mechanisms.

Needless to say, the thyroid function is dependent on iodine supply (Chs. 6 and 20). The thyroid holds $\frac{1}{3}$ to $\frac{1}{5}$ of the total (about 40 or 50 mg) body iodine in man. Iodine is taken up to saturation by the gland within 15 minutes after iodine-solution injection[244]. Thyroxine contains 65 per cent iodine; U.S.P. desiccated whole thyroid contains 0.17 to 0.23 per cent iodine. The iodine content of the thyroid is lowest in early spring and highest in late summer (Ch. 8). Iodine deficiency leads to thyroid abnormalities ranging from relatively harmless goiter to serious cretinism. Both of these and other thyroid abnormalities are found in man and animals depending on the iodine content of the soil in given geographical regions[245, 246], (Northwest, Mississippi Valley, Great Lakes, St. Lawrence Valley, the Andean plateau in South America) and in Europe (Alps, Pyrenees, Carpathians, also Himalayan Plateau in Asia). In these goitrous regions the diet of man contains less than 0.04 mg iodine per day; it should contain 0.1 mg (100 gamma), to maintain the body iodine at the optimum level of about 50 mg ($\frac{1}{5}$ of which is in the thyroid gland). The average human body contains, perhaps, 12 mg thyroxine.

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[237] Logras, G., and Drummond, J. C., *Biochem. J.*, **32**, 964 (1938). Belasco, I. J., and Murlin, J. R., *J. Nut.*, **20**, 577 (1940). Smith, D. C., and Perman, J. M., *Endocr.*, **27**, 110 (1940). Sheets, R. F., and Struck, H. C., *Science*, **96**, 408 (1942).

[238] Kunde, M., *Proc. Soc. Exp. Biol. Med.*, **23**, 812 (1926).

[239] Fellenberger, T., and Grueter, F., *Biochem. Z.*, **253**, 42 (1932).

[240] Belasco and Murlin[237], 1940.

[241] Aub, J. C., *et al.*, *J. Clin. Inv.*, **7**, 97 (1929); **10**, 187 (1931); **11**, 1273 (1932). Robertson, J. D., *Nature*, **148**, 724 (1941), and many others.

[242] Sturgis, C. C., and Greene, J. A., *Arch. Int. Med.*, **36**, 561 (1925). Ivy, A. C., *et al.*, *Am. J. Physiol.*, **139**, 139 (1943).

[243] Hisaw, F. L., *Anat. Rec.* (Suppl.), **67**, 50 (1936).

[244] Hertz, S., *Am. J. Physiol.*, **120**, 565 (1940).

While dietary deficiency of iodides—like that of chlorides—may be followed by serious physiologic disturbances, the opposite, namely, moderate dietary excess of iodide—like moderate dietary excess of chloride—is simply excreted, probably without physiologic disturbance. About 70 per cent excess dietary iodide is excreted in feces, the remainder in urine and, in dairy cattle, in milk[247]. Blood iodide may be increased ten times normal by dietary means with corresponding iodide increases in milk without apparent harm to the animal[247].

Thyroid abnormalities resulting from dietary iodine deficiency are now prevented by the use of iodized salt. This salt contains one part of NaI, or KI, in 5000 parts of salt (0.02 per cent, or one ounce in 300 lbs salt, or 1 part of iodine per million of salt[248]).

Iodine intake is not helpful in athyreosis. In this case, desiccated thyroid is fed or thyroxine is injected. When the basal metabolic rate is 20 per cent below average (in humans), 1 to 1$\frac{1}{2}$ grains (65 to 100 mg) U.S.P. thyroid is taken daily[249]. Cretins are given $\frac{1}{10}$ to 1 grain up to 4 years, 1–2 grains 4 to 12 years.

According to the review by Boothby and Saniford[250], the calorigenic effect of 1 mg thyroxine administered intravenously is about 1000 Calories. This value is based on the observation of the effect of a given dose on a given individual or set of individuals in a certain condition. But the calorigenic effect per mg thyroxine necessarily changes with increasing dosage level and varies with conditions. Thus Meyer and Wertz[251] reported that thyroidectomized animals are very much more sensitive than normal to a given thyroxine dose. The response tends to be inversely proportional to the initial level of metabolism.

An apparently curious aspect about thyroid administration is that it often improves not only the hypothyroid, but also the hyperthyroid individual. Thyroid administration was observed to lower the metabolism by 30 per cent (to normal) in some cases of hyperthyroid adenoma in exophthalmos[252].

B. Thyroid and adrenal medulla. Adrenaline, produced by the adrenal medulla, is related to thyroxine chemically as well as physiologically. Chem-

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[245] McClendon, J. F., "The distribution of iodine with reference to goiter," *Physiol. Rev.*, **7**, 189 (1927). Orr, J. B., and Leitch, I., "Iodine in nutrition," British Med. Res. Council, special report series, 123, 1929.

[246] Earlier papers on goiter: Marine, D., "Hyperplasia of the thyroid in dog, sheep, and man", *Johns Hopkins Hospital Bull.* **18**, 359 (1907). Welch, H., "Hairlessness and goiter in newborn domestic animals," Montana Agr. Exp. Sta. Bull. 119, 1917. Smith, G. E., "Fetal athyreosis," *J. Biol. Chem.*, **29**, 25 (1917). Hart, E. B., and Steenbock, H., "Hairless pigs", *Id.*, **33**, 331 (1918); Wis. Agric. Exp. Sta. Bull. 12, 1918. Kelkus, J. W., "Goiter and fetal athyreosis in farm animals," Washington Agr. Exp. Sta. Bull. 156, 1920. Mills, R. H., "Calf losses due to iodine deficiency," *J. Am. Vet. Med. Assn.*, **85**, 645 (1934).

[247] Meyers, J. H., Matthews, N. L., and Curtis, G. M., "The effects of increased iodine feeding to a herd of sixty dairy cows," *Ohio J. Sci.*, **40**, 9 (1940). Meyer, A. E., *et al.*, *Endocrinology*, **28**, 816 (1941).

[248] Committee on foods, *J.A.M.A.*, **99**, 1691 (1932).

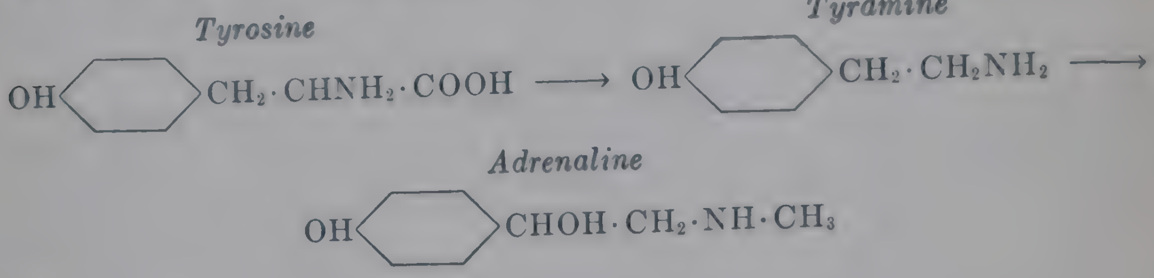
[249] Means and Lerman, *Arch. Int. Med.*, **55**, 1 (1933). See Du Bois[209], for details.

[250] Boothby, W. M., and Sandiford, I., "Basal metabolism," *Physiol. Rev.*, **4**, 69 (1924); *Proc. Staff Mayo Clin.*, **1**, 166 (1926).

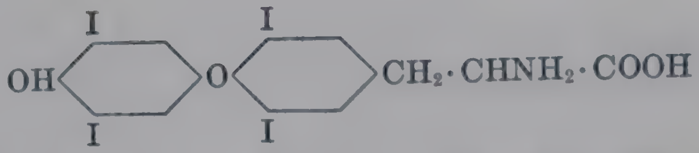
[251] Meyer, A. E., and Wertz, A., *Endocrinology*, **24**, 683 (1939).

[252] Salter, W. T., and Lerner, I. M., *Endocrinology*, **20**, 801 (1936).

ically, both are tyrosine derivatives, as indicated by the following. Adrenaline[253] may be thought of as derived from one molecule of tyrosine,



while thyroxine,



an aromatic ether, is derived from two molecules of tyrosine, with the elimination of the side chain of one[254].

While both adrenaline and thyroxine are metabolic (oxidation) catalysts, the time relations of their effects are different. The influence of the thyroid on metabolism is of the long-range steady type. The adrenal (medulla), on the other hand, influences metabolism under emergency conditions, controlling explosive outbursts of energy for short-time intervals. The adrenal medulla is a typical "alarm" gland.

It is generally accepted that there is close interrelation between the adrenal medulla and the sympathetic (autonomic) nervous system (Ch. 10). Thus splanchnic stimulation increases adrenaline secretion, whereas splanchnic removal decreases it. Stimulation of the sympathetic system by drugs, as metrazol, or by electric means, resembles the effect of adrenaline administration. The animal shows an emergency syndrome with such symptoms as increased blood pressure, pounding of heart, "standing-up" of hair, increase in respiration, shunting of the blood to the muscles, blanching of skin, and so on.

The large literature on the interrelations between the adrenal medulla and the sympathetic nervous system is best generalized by Cannon's[255] "emergency theory". According to this theory, under stress or emotion the physiologic resources are mobilized for action through the agency of adrenaline acting on the sympathetic system. The discharge of adrenaline into the circulation accelerates heart action, mobilizes glycogen, constricts blood vessels of skin and digestive system, thus making more blood available for muscles and nervous system. In the event that this mobilization for action is not followed by action, the mobilized sugar is excreted through the urine ("psychic glucosuria"). It was long known that fright (barking dog) induces glycosuria in the cat, and that attending exciting football games, or taking college examinations, is followed by sugar excretion[256] (Sect. 10.8).

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[253] For the original chemical papers, see Abel, J. J., "Method of preparing epinephrine," *Bull. Johns Hopkins Hospital*, **13**, 29 (1902). Aldrich, T. B., "The active principle of the suprarenal gland," *Am. J. Physiol.*, **5**, 457 (1901); Takamine, J., "Isolation of the principle of the suprarenal gland," *J. Physiol.*, **27**, 29 (1901-2). For a review of the literature, see Grollman, A., "The adrenals," 1936.

[254] The importance of the thyroid in metabolism was demonstrated about 1895 by Magnus-Levy. For the metabolic literature, see Du Bois, E. F., "Basal metabolism in health and disease." For the chemical aspects, see Kendall, E. C., "Thyroxine," New York, Reinhold Pub. Corp. 1929, and Harrington, C. R., "The thyroid gland, its chemistry and physiology," London, 1936. Kendall obtained an active principle of the thyroid in crystalline form in 1914. Harrington and Barger synthesized it in 1927.

[255] Cannon, W. B., Shohl, A. T., and Wright, W. S., *Am. J. Physiol.*, **29**, 280 (1911-12); Cannon and Britton, S. W., *Id.*, **79**, 433 (1926-27); Cannon, "The wisdom of the body," New York, 1932; "Bodily changes in pain, hunger, fear and rage," Appleton, 1929,

While the adrenal medulla (and adrenaline secretion) is highly responsive to the nervous system (to the medullary, hypothalmic, and spinal centers), the thyroid is relatively unresponsive. The thyroid function is of the long-range steady type, contrasted to the emergency-explosive type of nervous reaction of the adrenal medulla.

There may be associated with this relative functional difference between the adrenal and thyroid, a relative size difference. To quote from Robert Crile[257], "the relative sizes of the adrenal and thyroid glands of animals might vary according to the energy characteristics and habits of the animals". The thyroid size in continuously sensitized man is about twice that of the adrenal size; the adrenal size in rodents, which rely on explosive outbursts of energy for survival, is about 23 times that of the thyroid.

C. Thyroid and anterior pituitary. As previously explained, the thyroid is under the control of pituitary thyrotropic hormone[258] in the same manner that the gonads are under the control of pituitary gonadotropic hormone. Administration of the pituitary thyrotropic extract increases heat production (by action on thyroid) by 30 per cent[259] to 60 per cent[260]. The thyrotropic hormone may be assayed by increase in heat production[259, 260], increase in size of the thyroid of the guinea pig[261], and/or the chick[262, 263]. The anterior pituitary may also have a metabolism-accelerating principle which acts independently of the thyroid[264], but this is not certain[265].

The pituitary and thyroid hormones appear to be synergistic or complementary in their effects on growth and development[266]. The thyroid hormone "primes" or "tones" the tissues for the action of the pituitary growth hormones[267]. It appears, moreover, that sufficiently early thyroidectomy inactivates the pituitary so that the animal becomes virtually hypophysectomized as well as thyroidectomized[268].

D. Thyroid and posterior pituitary. A curious observation[269] relating the thyroid to the posterior pituitary concerns a polyuria (diabetes insipidus) produced by placing a clip on the stalk of the pituitary. This polyuria is abolished by removing the thyroid, and returned by feeding thyroid to the animal (dog).

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[256] Folin, O., Denis, W., and Smillie, W. G., *J. Biol. Chem.*, **17,** 519 (1914); Malmiwirta, F., and Mikkonen, H., *Skand. Arch. Physiol.*, **45,** 68 (1924).

[257] Crile, R., *Ohio J. Sci.* **37,** 42 (1937). Crile, George, "Intelligence, power and personality," McGraw-Hill Book Co., 1941.

[258] Collip, J. B., *J.A.M.A.*, **115,** 2073 (1940).

[259] Collip, J. B., and Anderson, E. M., *Id.*, **104,** 965 (1935).

[260] Seibert, W. J., and Smith, R. S., *Proc. Soc. Exp. Biol. Med.*, **27,** 622 (1933).

[261] Loeb, L., and Bassett, R. B., *Proc. Soc. Exp. Biol. Med.*, **27,** 490 (1930).

[262] Smelzer, G. K., *Id.*, **37,** 388 (1937).

[263] Bergman, A. J., and Turner, C. W., *Endocrinology*, **24,** 656 (1939).

[264] O'Donovan, O. K., and Collip, J. B., *Id.*, **23,** 718 (1938).

[265] Chambers, W. H., Shorr, E., and Barker, S. B., *Ann. Rev. Physiol.*, **4,** 155 (1942).

[266] Evans, H. M., Simpson, M. E., and Pencharz, R. E., *Endocrinology*, **25,** 175 (1939).

[267] Salmon, T. N., *Id.*, **29,** 291 (1941).

[268] Severinghaus, A. E., *Cold Spring Harbor Symposia on Quantitative Biology*, **10,** 107 (1942).

[269] Mahoney, W., and Sheehan, D., *Am. J. Physiol.*, **112,** 250 (1935).

E. Thyroid and gonads. Thyroidectomy arrests sexual development (Fig. 7.5), and reduces energy metabolism; gonadectomy also reduces energy metabolism and reduces the thyroid. On the other hand, administration of sex hormone increases basal metabolism[270]. Puberty and pregnancy also enlarge the thyroid[271], perhaps by pituitary thyrotropic hormone stimulation[272].

As previously noted, the relation between thyroid and gonad is not fully clear, especially as it relates to rats. Lee[273] reported that thyroidectomy of young rats did not seriously delay puberty but lengthened the estrus cycles. Hammett[274], likewise, found no relation between thyroid activity and development of the reproductive system and suggested that the reported disturbed sex conditions are secondary to disturbed *general* growth, not to specific sex disturbance. But this depends on age of thyroidectomy. In our experience on cattle and goats early thyroidectomy arrests sex development completely. The discrepancies may be due to differences in physiologic age at thyroidectomy.

F. Thyroid and central nervous system. Attention has been called to the interrelation between "emergency" emotions, adrenal and thyroid, and to the influence of thyroid on nerve metabolism, on neuromuscular irritability and on variability. All this is, of course, equivalent to saying that there is an interrelation between thyroid, adrenal, and nervous system. By way of further evidence, one may note that the thyroid gland appears to be heavier in emotional than in non-emotional rats[275], and that certain types of insanities ranging from "amazing placidity" and profound depression to high excitability, irritability, and anxieties are often improved by either thyroid administration or thyroid depression[276]. Ten per cent of the sufferers from dementia praecox are hypothyroid and most benefit from thyroid medication.

On the other hand, manic-depressive swings in mood in psychotic persons are often associated with swings in blood iodine[277]. In brief, while hypo- or hyperthyroidism is probably not the "cause" of psychotic conditions, it may

[270] Thompson, W. O., and Heckel N. J., *J.A.M.A.* (1939) reported 30 per cent increase in metabolism following administration of 100 mg testosterone propionate to enunchoid men.

[271] Marine, D., *Ohio J. Sci.*, **37**, 408 (1937). Portes, B., and Roth, H. A., *J.A.M.A.*, **115**, 895 (1939).

[272] Marine, D., *J.A.M.A.*, **104**, 2250 (1935).

[273] Lee, M. O., *Endocrinology*, **9**, 410 (1925).

[274] Hammett, F. S., *Quart. Rev. Biol.*, **4**, 353 (1929).

[275] Yeakel, E. H., and Rhoades, R. P., *Endocrinology*, **28**, 337 (1941).

[276] Hoskins, R. G., "Endocrinology," Norton, 1941. Carmichael, H. T., *J. Abn. Social Psychology*, **33**, 205 (1938). Brown, W. T., and Gildea, E. F., *Am. J. Psychiatry*, **94**, 59 (1937).

[277] Neustadt, R., and Howard, L. B., "Fluctuations in blood iodine in cyclic psychoses," *Am. J. Psychiat.*, **99**, 1930 (1942).

influence it, and the thyroid, in turn, may be influenced by the sensitiveness or instability of the nervous system.

It is of course obvious that cretinism includes arrested development of the central nervous system, that is, an arrested "mind", and this condition is often prevented by beginning thyroid medication at a sufficiently early age, provided of course the "residual physiologic capacity and latent growth potency of the neuroendocrine system"[278] are adequate.

Many remarkable cases of psychiatric interest could be cited. One from Means[279], concerns a mentally normal and unusually intelligent child of ten years who showed typical myxedema. On administration of thyroid which cured the myxedema, she developed a "mental decompensation", a severe manic-depressive psychosis. The psychosis disappeared on removing the thyroid medication but the myxedema returned. This result of benefiting one function and injuring another obviously has applications in agriculture as in medicine.

Then, too, according to Means, severe fright or worry may touch off a latent thyroid abnormality; for example, an exophthalmic goiter may develop in two or three days. Usually such development occurs gradually during a prolonged period of anxiety, sorrow, strife, or fear. The same may be touched off by acute infection, pregnancy, parturition, puberty, menopause, and other crises. On the other hand, many latent psychoses (manic depressive, acute delirium, toxic exhaustion, and so on) are brought on by toxic goiter[280].

One could discuss the many theories of the influence of thyroid activity on human social leadership. But for our purpose the following is sufficient. Allee[281] observed that thyroid administration to hens at the highest "social level" caused loss in their "social order" in the flock if the thyroid caused them to moult. A lower thyroid dosage level did not affect their "social position", contrasted to the effect of raising birds in the social (aggressive) position following low dosages of testosterone propionate. The dosage level is very important in hormone effect.

What was said about the influence of the thyroid on the central nervous system could be said, if space permitted, about the adrenals and the other glands.

7.3.3: Some applications and summary of thyroid endocrinology. The thyroid resembles the pituitary in influencing all other endocrines. Pituitary control is by specific tropic hormones, but thyroid control is largely non-specific. The essential thyroid effect is, then, to accelerate the speed of all life processes, including those of the other endocrine glands and those of agricultural importance: milk production, egg production, and in some cases growth and reproduction.

The acceleration is not only for anabolic (building up) but also for catabolic (breaking down) and senescence processes. Thyroid administration can thus be practically helpful when the natural thyroxine production by the given animal is below the level required for optimal efficiency. Some individuals and even species are slightly hypothyroid by nature; in such cases slight thyroid administration may be helpful. We have thus seen that the growth rate of some strains of mice and of some humans is accelerated by thyroid administration, but not that of the rats, guinea pigs, and rabbits investigated, nor of most humans.

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[278] Gesell, A., *et al.*, *Am. J. Dis. Child.*, **52**, 1117 (1936). See also Wilkins, L., *et al.*, *J. Clin. Endocrinology*, **1**, 3 (1941). "Thyroid medication in childhood," *J.A.M.A.*, **114**, 2382 (1940).

[279] Means[209].

[280] Dunlap, H. F., and Moersch, F. P., *Am. J. Psychiat.*, **91**, 1215 (1935).

[281] Allee, W. C., *et al.*, *Endocrinology*, **27**, 827 (1940).

Under certain conditions and at certain times (in the declining phase of the lactation period), the rate of milk production may be increased by thyroid administration at low levels. The question whether the milk-production efficiency (ratio of milk produced to feed consumed) is increased or decreased by the accelerated milk production has not yet been answered. Nor has it been determined how increasing the tempo of living by the thyroid administration affects the fertility and longevity of the animal, or its future usefulness. Under certain conditions the question of future usefulness does not enter; it is thus of little importance whether or not an animal's fertility or longevity is affected in the remote future by thyroid administration if it is planned to slaughter the animal in the near future.

7.4: Adrenal cortex. As outlined above, the adrenal gland consists of a medulla (central portion) which is associated with the sympathetic nervous system, and produces adrenaline; and a cortex (shell) which is associated with the reproductive system and produces some 20 steroids[283] similar in structure to sex hormones (Fig. 7.1), collectively referred to as *cortin*[284]. Addison's disease (described by Thomas Addison in 1855) is due to atrophy of the adrenal cortex (usually by local tuberculosis). The adrenal cortex extract cortin or the steroids isolated therefrom (more recently synthesized) function successfully in replacement therapy when the adrenal cortex is removed or atrophied.

There is some functional relation between the adrenal cortex and adrenal medulla, in that cortin probably stimulates the sympathetic nervous system to conduct impulses to the medulla[285], and that both are involved in carbohydrate metabolism[286]. Adrenaline is not physiologically essential for life maintenance (it appears to be useful only in emergency), but cortin is. Lack of cortin leads to profound hypoglycemia[287], loss of sodium chloride[287] and water, to potassium retention[287], low blood pressure, weak heart action, reduced basal metabolism (by about 25 per cent), disturbed temperature regulation, and general muscular weakness. The two most obvious adrenal-cortex functions are, then, salt and water balance[288] and maintenance of the blood sugar level by gluconeogenesis[289] (sugar formation from protein). Two adrenal-cortex steroids, 11-dehydrocorticosterone and 17-hydrocorticosterone, are apparently involved in both salt and blood-sugar regulation. The particularly potent salt-regulating steroid is desocorticosterone[288] and the particularly potent carbohydrate former is corticosterone[289]. Both of these steroids were isolated and synthesized (1937) by Reichstein (Zurich), but Kendall and Mason and Wintersteiner and Pfiffner (U. S. A.) made outstanding chemical contributions and elucidated the relations between the many steroids.

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[283] For the history and chemistry of the adrenal-cortex hormones and their relation to sex hormones, see Pfiffner, J. J., *Advances in Enzymology*, **2**, 325 (1942).

[284] Hartman, F. A., *et al.*, *Proc. Soc. Exp. Biol. Med.*, **25**, 69 (1927); *Am. J. Physiol.*, **86**, 353 (1928). Rogoff, J. M., and Stewart, G. N., *Science*, **66**, 327 (1927).

[285] Secker, J., *J. Physiol.*, **94**, 259 (1918); **95**, 282 (1919).

[286] *Cf.* Long, C. N. H., *Endocrinology*, **30**, 870 (1942). Kendall, E. C., *Id.*, p. 853. Hartman, F. A., *Id.*, p. 861. See also Hartman, *J.A.M.A.*, **117**, 1405 (1941). Kendall, *Id.*, **116**, 2394 (1941). Collip, *Id.*, **115**, 2073 (1940). Ingle, D. J., and Lukens, F. D. W., *Endocrinology*, **29**, 443 (1941). Dill, D. B., *et al.*, *Am. J. Physiol.*, **121**, 549 (1938), and others. See also a series of articles by Hartman, Kendall, Grollman, *et al.*, in *Cold Spring Harbor Symposia Quant. Biol.*, **5**, (1937).

[287] In 100 cc blood from normal individuals, there are about 330 mg Na, 600 Cl, 19 K, and 85 sugar; blood from patients with Addison's disease contains about 250 mg Na, 450 Cl, 26 K, and 50-60 sugar.

The sugar-forming potency of corticosterone (and to a less extent of 11-dehydrocorticosterone and 11-dehydro-17-hydrocorticosterone) is great enough to induce severe glucosuria[290] on its administration.

In the absence of cortin or its active steroids, life may be maintained in Addison's disease (or adrenalectomy) by increasing the intake of sodium salt, the amount depending on the condition (edema, etc.) and reducing intake of potassium salt; to overcome the tendency to hypoglycemia, and consequent muscular weakness, increase the carbohydrate intake. Hartman outlined methods for measuring cortin deficiency and emphasized the extra cortin demands in conditions of stress, "infections, toxins, shock, great heat, great cold, exercise"[291].

The fact that extra cortin is needed under conditions of stress does not mean that it would benefit normal animals to have extra cortin. Indeed, as in the case of thyroxine, the opposite may be true, depending on dosage and sensitivity of the animal. As on administration of excess thyroxine or thyrotropic hormone, so on administration of excess cortin or adrenotropic hormone there is increase in the catabolic rate, especially of protein deamination and urinary nitrogen excretion. The excessive deamination is associated with excess sugar formation and excretion. The effect on nitrogen metabolism and on growth is opposite to that of pituitary growth-hormone administration[292] (which increases protein anabolism and reduces nitrogen excretion). There appears to be a reciprocal relation of the pituitary-growth and adrenal-cortical hormones in their effect on protein metabolism[292, 293].

It is interesting to note (Fig. 17.5) that on approaching maturity, when the rate of total body gain declines rapidly, the rate of weight gain of the adrenal cortex increases rapidly until total weight gain is brought to a standstill. The adrenal cortex activity may be the limiting factor in bringing growth to a standstill (C. W. Turner). Would removing part of the adrenal cortex permit further growth? The adrenal-cortex spurt in growth coincides with the gonad spurt in growth, and the sex hormones, at any rate estrogen, are known to depress the growth-promoting properties of the anterior pituitary[294]; dwarfing of rats and chickens was produced by administration of follicular hormone[294]. Corticosterone (not desocorticosterone) is particularly effective in repressing lymphoid tissue[295] (thymus, lymph nodes). Corticosterone or cortin administration, of course, atrophies the adrenal cortex by repressing liberation of corticotropic hormone[296]. Under stress adrenotropic hormone output is increased and the adrenal is hypertrophied. The level of cortin metabolism apparently parallels that of basal metabolism.

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[288] Loeb, R., *Science*, **76**, 420 (1932); *J. Exp. Med.*, **57**, 775 (1933). Thorn, G. W., *et al.*, *Id.*, **94**, 348 (1941).

[289] Long[286]. Long and Katzin, B., and Fry, E. G., *Endocrinology*, **26**, 309 (1940).

[290] Ingle, D. J., *Am. J. Physiol.*, **133**, 337 (1941); **132**, 670 (1941). Thorn, G. W., *et al.*, *J. Clin. Inv.*, **19**, 813 (1940).

[291] Hartman, F. A.[286]. There is a large literature on shock. For a review, see Rubin, S. H., *et al.*, Macy Foundation, 1941. Schleser, I. H., and Asher, R., *Am. J. Physiol.*, **183**, 1 (1942). Swingle, W. W., *et al.*, *Am. J. Physiol.*, **139**, 481 (1943).

[292] For review of the literature, see Tepperman, *et al.*, *Endocr.*, **32**, 373 (1943), and Long[286].

[293] Long, C.N.H., *Cold Spring Harbor Symposia on Quantitative Biology*, **10**, 98 (1942). Marx, W., Simpson, M. E., *et al.*, *Endocrinology*, **33**, 102 (1943).

Just as the basal metabolism per unit weight is greater in small than in large animals (Chs. 13 to 15), so is the cortin need per unit weight. A rat needs 40 times and a cat 4 times as much cortin per unit body weight as man (Hartman). The importance of the adrenal-cortical function in metabolism is indicated by hypertrophy of one adrenal if the other is removed, and the fact that such hypertrophy is avoided by administration of adrenal-cortical extract. Also, newly-born of adrenalectomized mothers show abnormally large adrenals[297].

As previously explained, sex hormones and adrenal-cortex hormones are related structurally (Fig. 7.1) and functionally. Gonad removal hypertrophies the adrenal cortex[298], while sex-hormone administration reduces the adrenal cortex. Progesterone is said to atrophy the adrenal cortex of male rats[299], although this problem is still under investigation. Estrogen, however, is said to have the opposite effect—adrenal hypertrophy—and therefore increase in protein catabolism and suppression of growth. The "infant Hercules" type of precocious sexual and muscular development is associated with adrenal-cortex tumor; so is virilism in women[300] (the circus' "bearded lady"); and perhaps some types of feminism in men may be attributed to adrenal-cortex dysfunction. Conversely[301], sex hormones, or hormone-like bodies, particularly progesterone and stilbestrol, may substitute for some adrenal-cortex hormones by causing sodium-ion retention and potassium-ion excretion.

Riddle[302] reported that adult pigeons and doves "showed male behavior to an extent equalling that of any normal bird that I have ever observed", yet "these birds never possessed a gonad". The male behavior of these gonad-less birds is attributed to adrenal-cortical male hormone production, said to be produced by a special *androgenic tissue*, associated with the adrenal cortex. Pseudo-male hermaphrodism with male behavior and functional prostatic tissue in the absence of testicular tissue is attributed to androgen production by this androgenic adrenal tissue[303].

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[294] Zondek, B., *Lancet*, **2**, 842 (1936).

[295] Wells, B. B., and Kendall, E. C., *Proc. Staff Meet. Mayo Clinic*, **15**, 133 (1940).

[296] Ingle, D. J., *Am. J. Physiol.*, **124**, 369 (1938)

[297] Tepperman, Engel and Long[290].

[298] Sandberg, N., *et al.*, *Endocrinology*, **24**, 503 (1939).

[299] Clausen, H. J., *Endocrinology*, **27**, 989 (1940).

[300] Wintersteiner, O., *J.A.M.A.*, **116**, 2679 (1941). Lukens, F. D. W., and Palmer, H. D., *Endocrinology*, **26**, 941 (1940).

[301] Emery, F. E., and Greco, P. A., *Endocrinology*, **27**, 473 (1940). Miller, H. C., *Id.*, **32**, 443 (1943).

[302] Riddle, O., *Cold Spring Harbor Symposia on Quant. Biol.*, **5**, 320 (1937).

Not only sex hormone but also lactation hormone (cortilactin) was prepared (by isoelectric precipitation) from the adrenal cortex[304]. This stimulates the crop sac of pigeons similar to (pituitary) prolactin (Sect. 7.2).

Richter[305] called attention to the influence of adrenalectomy on appetite behavior (Chs. 10 and 20). Removal of the adrenals is followed by excessive loss of sodium chloride and also by a compensating appetite for salt. A boy who had excessive craving for salt was found to have an adrenal cortex eroded by a tumor. Conversely, adrenal (and other) abnormality may often be inferred from observation of the appetite.

Glutathione is said to be involved in growth acceleration (Chs. 6 and 16), and it may be significant that adrenal tissue is richest in glutathione[306].

As noted in the introduction, the adrenal cortex is interrelated with the anterior pituitary adrenocorticotropic hormone, with the pituitary occupying the "controlling" position. This is indicated by adrenal cortex atrophy on pituitary removal (the atrophy is greater than could be caused by thyroid deficiency), and adrenal restoration to normal on pituitary implantation[307]. The effect on the microscopic picture of the adrenal medulla appears within 2 hours after the pituitary administration[308]. Under some conditions A.P. administration may depress the catabolic effect of the adrenal cortex (and thus accelerate growth)[309]. Under other conditions A.P. administration may lead to adrenal hypertrophy (70–130%)[310]; conversely, adrenalectomy or adrenal administration affects the pituitary[311]. Preparation of pituitary adrenotropic hormone was recently reported[312].

In addition to the interrelation of the adrenal cortex to the pituitary and gonads, it is also related to other endocrines, such as the thyroid. Hyperthyroidism leads to hypertrophy of the adrenal cortex[313], perhaps as a result of increased metabolism. Apparently anything that increases metabolism (including lactation) hypertrophies the adrenal cortex. Then, too, it is said that the adrenal cortex exercises an inhibiting control over the thyroid[314]. Individuals with hypofunctioning adrenals are particularly sensitive to thyroxine, leading to "hyperthyroid crisis"[315] on thyroid administration.

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[303] Grollman, *Id.*, p. 318.

[304] Hartman, *et al.*, *Am. J. Physiol.*, **134**, 12 (1941).

[305] Richter, C. P., *Ann. Rev. Physiol.*, **4**, 561 (1942). See also Clark, W. G., and Clausen, D. F., *Am. J. Physiol.*, **139**, 70 (1943).

[306] Hammett, F. S., *Protoplasma*, **7**, 535 (1929).

[307] Smith, P. E., *Am. J. Anat.*, **48**, 205 (1930).

[308] Anselmino, K., *et al.*, *Klin. Woch.*, **13**, 1724 (1934).

[309] Young, F. G., *Brit. Med. J.*, **2**, 897 (1941). Mirsky, I. A., *Endocrinology*, **25**, 52 (1939).

[310] Emery, F. E., and Atwell, W. J., *Anat. Rec.*, **58**, 17 (1933). Ingle[236].

[311] Shumacher, H. B., *Endocrinology*, **18**, 676 (1934).

[312] Sayers, G., White, A., and Long, C. N. H., *Proc. Soc. Exp. Biol.*, **52**, 199 (1943). Li, C. H., Evans, H. M., and Simpson, M. E., *J. Biol. Chem.*, **149**, 413 (1943).

[313] Korenchevsky, V., and Hall, K., *Biochem. J.*, **35**, 726 (1941). Ingle, D. J., and Higgins, G. M., *Endocrinology*, **23**, 419 (1938).

[314] Marine, D., Bauman, E., *Am. J. Physiol.*, **57**, 135 (1921); **59**, 353 (1922). Scott, W. J. M., *J. Exp. Med.*, **36**, 199 (1922).

[315] Perea, G. A., and Parker, D. D., *J.A.M.A.*, **122**, 669 (1943).

Summarizing, the adrenal cortex produces hormones similar to sex hormones. It is especially associated with the regulation of salt and water metabolism and with carbohydrate and protein metabolism, and therefore with growth, lactation, and related productive processes. Because of its effect on carbohydrate metabolism, especially gluconeogenesis, the adrenal cortex function may, perhaps, be a limiting factor in milk production. Relative hypofunction of the adrenal cortex in comparatively high-milking animals may, perhaps, lead to the hypoglycemic type of milk fever. On the other hand, hyperfunction of the adrenal cortex may cause inefficient feed utilizaion and growth depression. The field is at present under intensive investigation, the results of which explain many phenomena, and find use in medicine; but they have not yet been carried to the point of application in agriculture.

7.5: Calcium-phosphorus metabolism hormones: the parathyroids[316].—As previously noted, all hormones are metabolic catalysts, but some, like the thyroids, are best known for their catalytic effect on energy metabolism, although the effect is no less apparent on calcium metabolism[317]. The gonads are best known for their effect on sex activity, although they, too, catalyze calcium metabolism, which is certainly true as regards the effect of estrogen on calcium storage, on blood calcium in birds[318], and on bone metabolism and strength[319]. On the other hand, ovariectomy often leads to hypocalcemia[320]. The adrenal cortex is best known for its effect on energy and carbohydrate metabolism and on maintenance of muscular efficiency, although it has an equal effect on sodium retention and on electrolyte balance. Likewise, the parathyroids (Fig. 17.30) are best known for their effect on calcium and phosphorus metabolism; by controlling this, they may be said to regulate growth and related productive processes[321].

The word "control" (of calcium metabolism) is perhaps too strong for characterizing the parathyroid effect on calcium metabolism; "regulation" is better. Just as adrenalectomized animals may be maintained under quiet conditions by administration of extra salt, water, and carbohydrate, so parathyroidectomized animals under quiescent conditions (not pregnant or lactating) may be maintained by administration of extra calcium and vitamin D.

Calcium occupies an extremely important position in the body economy in general, and in growth, milk and egg production in particular. About 2 per cent of the body is calcium and 99 per cent of this calcium is in the skeleton[322]. While support is one of its obvious functions, the skeleton is not merely an inert supporting structure. The skeleton is, on the contrary, like other constituents of the living body, in rapid flux[323]. The calcium in bone is interrelated with the calcium-ion level in the blood, as body glycogen is interrelated with the glucose level in the blood (Sects. 10.4 and .5).

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[316] Campbell, I. L., and Turner, C. W., Univ. Missouri Agr. Exp. Sta. Res. Bull. 352, 1942. Dragstedt, L. R., *Physiol. Rev.*, **7**, 499 (1927). Hess, A. F., "Rickets and tetany," Lea & Febiger, 1929. Huggins, C., *Physiol. Rev.*, **17**, 119 (1937). Kay, H. D., *Id.*, **12**, 384 (1932). Logan, M. A., *Id.*, **20**, 522 (1940). Schmidt, C. L. A., and Greenberg, D. M., *Id.*, **15**, 297 (1935). Shelling, D. H., "The parathyroids in health and disease," Mosby, 1935. Thompson, D. L., and Collip, J. B., *Physiol. Rev.*, **12**, 309 (1932). A recent, shorter review: Albright, F., *J.A.M.A.*, **117**, 527 (1941).

[317] Aub[241], and *Harvey Lectures*, **24**, 151 (1928–29).

[318] Riddle, O., and Dotti, L. B., *Science*, **84**, 557 (1936); *Am. J. Physiol.*, **123**, 171 (1938); Riddle, *Ann. Rev. Physiol.*, **3**, 573 (1941). Bloom, M. A., and McLean, F. C., *Anat. Rec.*, **83**, 99 (1942) (testosterone synergizes with estrogen in stimulating bone formation).

[319] Gardner, W. U., *Endocrinology*, **32**, 149 (1943); *Physiol. Rev.*, **23**, 139 (1943).

[320] Shapiro, H. A., and Zwarenstein, J., *J. Exp. Biol.*, **10**, 186 (1933).

[321] Sherman, H. C., and MacLeod, F. L., *J. Biol. Chem.*, **64**, 429 (1925).

The calcium-ion level in the blood is the resultant of dietary calcium and vitamin D, calcium outgo (into bone, milk, egg, etc.), and parathyroid hormone level (Ch. 20).

Normally, the blood serum or plasma contains about 10 mg per cent of calcium (in whole blood about 5 mg per cent) half of which—about 5 mg per cent—is in the form of calcium ion and the other half as calcium proteinate. On parathyroid removal, the blood-serum calcium declines to about half normal (5 mg per cent) and the organic phosphorus rises to about 25 per cent above normal (from about 5 to about 7.5 mg per cent). On injecting parathormone (or on overactivity of the parathyroid, usually due to tumor) the opposite occurs—the blood calcium level may be doubled and the organic phosphorus level may be halved. The quantitative effect is analogous to that of thyroid removal and thyroid administration.

The detailed mechanisms whereby these changes are brought about are at present under investigation. Unlike the thyroid, the parathyroid does not appear to be under pituitary control[324]. In addition to the calcium mobilization from bone, parathormone, like cortin, may exert an effect on selective kidney function.

The calcium factor is particularly important in the dairy industry not only because calcium is one of the most valuable dietary constituents in milk, but also because it is often a limiting factor in milk production. The blood-calcium level in high-milking cows may decline to very low levels with the resulting dangerous "milk fever" (just as the blood-sugar level may decline to abnormally low level in adrenal hypofunction or in low carbohydrate intake, causing "milk fever"). Under such or similar conditions, when the calcium outgo into the milk greatly exceeds the income from feed, the parathyroid is hypertrophied in the performance of its function of mobilizing the bone calcium[325]. But in spite of the hypertrophy, the blood calcium may decline during heavy lactation and, in some species, during the later phases of gestation. The low blood calcium in milk fever is probably not the result of low dietary calcium, but of the inability of the digestive, assimilatory and calcium-mobilizing mechanisms to keep up with the milk-secreting mechanisms.

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[322] *Composition of bone:* 60 per cent is ash; of the bone ash, 80 per cent is $Ca_3(PO_4)_2$, 13 per cent is $CaCO_3$, 2 per cent is $Mg_3(PO_4)_2$; or 36 per cent of the ash is Ca, 16 per cent is P; 0.5 per cent is Mg, and 5.5 per cent is CO_2. It turns out that the Ca to P ratio is about 2 to 1, and that the $Ca_3(PO_4)_2$ to $CaCO_3$ ratio is about 1 to 1.5.

[323] Schoenheimer, R., "The dynamic state of body constituents," Harvard Univ. Press, 1942.

[324] Carnes, W. H., *et al.*, *Am. J. Physiol.*, **139,** 188 (1943).

[325] Marine, D., *Proc. Soc. Exp. Biol. Med.*, **11,** 117 (1914). Pappenheimer, A. M., and Minor, J., *J. Med. Res.*, **42,** 391 (1921). Ham, A. W., *et al.*, *Am. J. Path.*, **16,** 277 (1940). Roberts, E., *Anat. Rec.*, **79,** 417 (1941). Campbell and Turner,[316] 1942.

While dairymen would like to develop a more efficient parathyroid in cattle, or a parathyroid hormone suitable for administration to cattle to avoid milk fever, the cure might be worse than the remedy. Increasing the parathyroid efficiency might weaken the bones and deteriorate the teeth. The organismic-homeostatic viewpoint does not encourage parathyroid hormone administration to normal animals just as, as a rule, it does not encourage the administration of other hormones unless the animal is particularly deficient in some one hormone as contrasted to the abundance of other factors.

Fortunately, as previously noted, the calcium-ion level in the blood is a function not only of the parathyroid-hormone level but also of calcium and vitamin D intake in proper form[306]. The purely practical problem of avoiding milk fever, therefore, seems to be nutritional—supplying a high level of dietary calcium in proper form and vitamin D (irradiated yeast now available in inexpensive form)[327]. It appears[328] that milk fever in dairy cattle is decreased by feeding them a million I.U. units vitamin D (irradiated yeast) 30 days before and 10 days after calving.

The overall parathyroid function is to maintain constant the calcium-ion level in the blood serum, if necessary by removing the calcium from bones. By decalcification of bone under adverse conditions of dietary calcium supply, excess parathyroid aggrevates rachitic processes. Hyperparathyroidism causes serious bone disease. Vitamin D, on the other hand, promotes calcium deposition into the bone, if necessary by lowering the blood calcium. In brief, while the primary function of the parathyroid hormone is to maintain constant the calcium level in blood, that of vitamin D is to deposit calcium in the skeleton, which necessitates its removal from the blood. The two processes are balanced in a normal well-fed animal. The effect is opposite on serum phosphorus: parathyroid hormone depresses the serum phosphorus, vitamin D raises it.

While under conditions of dietary calcium deficiency vitamin D may, theoretically, reduce the blood calcium level by building it into bone, it ordinarily has a calcemic effect; it increases the blood calcium level by increasing the calcium absorption from the digestive tract. Indeed, in case of parathyroid deficiency, vitamin D_3 (7-dehydrocholesterol, from fish livers), vitamin D_2 (calciferol, an activated ergosterol) and dihydrotachesterol ("A.T.10", also an activated erogosterol derivative) tend to maintain the blood calcium at a normal level[329]. A.T. 10 increases the blood calcium level but, unlike vitamin D, is not antirachitic.

The obvious prophylactic against hypocalcemic milk fever and rickets seems to be to

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[326] McLean, F. C., *J.A.M.A.*, **117**, 609 (1941); Campbell and Turner[316].

[327] *Cf.* Hart, E. B., *et al.*, *J. Biol. Chem.*, **62**, 117 (1924); **71**, 271 (1927). Macy, I. G., *et al.*, *Id.*, **86**, 59 (1930). Henderson, J., and Magee, H. E., *Bioc. J.*, **20**, 363 (1936).

[328] Monroe, C. F., Krauss, W. E., and Sutton, T. S., "Control of milk fever," *Proc. Am. Dairy Sci. Assn.*, 37th Meet., 1942.

[329] McLean[326]. "There is a species difference in the calcemic effects of the 3 substances. Thus vitamin D_3 is equivalent to 40 000 U.S.P. units/mg for both rat and chicken; but while vitamin D_2 is equivalent to 40,000 units/mg in the rat, it is only 1000 units/mg in the chicken; crystalline dihydrotachysterol is equivalent to 80 U.S.P. units in the rat and 360 in the chicken. In the chick vitamin D_3 is 35 times as effective as vitamin D_2 and dihydrotachysterol is 4.5 times as effective as vitamin D_3." E. W. McChesney, *J. Nut.*, **26**, 81 (1943).

feed a high level of calcium in available form and irradiated yeast which, incidentally, also increases the vitamin D level in milk.

The growth of knowledge of the anatomy of the parathyroids parallelled that of the thyroids, beginning with about 1880 (Sandstrom). The relation of the parathyroids to nervous symptoms has been known since about 1890 (Horsley, Gley, Kohn), although it was not until 1908 that McCallum and Voegtlin[330] discovered that parathyroid removal in dogs is followed by abnormally low blood calcium and by "twitching, rigidity, tachypnoea, fibillary tremors, increased rapidity of the heart beat, etc.", all of which are overcome by intravenous injection of a 5 per cent solution of calcium acetate or lactate.

This definitely established the fact that the parathyroids regulate calcium metabolism. By 1925 potent parathyroid extracts had been prepared, especially by Collip[331], which substituted for the parathyroid in parathyroidectomized animals and caused hypercalcemia in normal animals[332].

Much incidental information gradually accumulated, such as that the decline in blood calcium is associated with an increase in blood phosphorus[333] (there tends to be a constant product of calcium and phosphate ions; the Ca/P ratio tends to be between 1 and 2, so that the proper functioning of the calcium metabolism is also dependent on a certain phosphate concentration[334]); that meat[335] aggravates and milk (or lactose[336]) helps in maintaining parathyroidectomized animals. At the same time the nutritional literature[337], as well as the hormonal, indicates that lactose ingestion exerts favorable influence on calcium assimilation, as does a proper Ca/P ratio. Anything that decreases the solubility of calcium salts (as excess oxalates, phosphates, alkalinity) decreases calcium absorption.

The importance of ionic balance ("ionic antagonism") on neuro-muscular irritability and permeability, especially in relation to calcium ions, has been long known[338], and also its widespread influence as, for example, on blood clotting, milk clotting, digestion, and so on. The same is true as regards phosphorus, which is not only a part of bone and every cell but is important in intermediate metabolism (phosphorylation, see Ch. 6). The same substance, calcium or phosphorus, seems to be used for many different purposes in the body and deficiency exerts correspondingly widespread effects.

7.6: Carbohydrate-fat metabolism hormones[339]. There is a similarity of pattern in the anatomy, physiology, and even in the history of our knowledge of the various endocrines and hormones and their interrelations.

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[330] MacCallum, W. G., and Voegtlin, C., *Bull. Johns Hopkins Hosp.*, **19**, 91 (1908); *J. Exp. Med.*, **11**, 118 (1909).

[331] Collip, J. B., Clark, E. J., and Scott, J. W., *J. Biol. Chem.*, **63**, 439 (1925); **64**, 485 (1925). Hanson, A. M., *Proc. Soc. Exp. Biol. Med.*, **22**, 560 (1925). Berman, L., *Id.*, **21**, 465 (1924). Hjort, A. M., *et al.*, *J. Biol. Chem.*, **65**, 117 (1925). Fisher, N. F., and Larson, E., *Am. J. Physiol.*, **75**, 93, 195. Tweedy, W. R., *Proc. Soc. Exp. Biol. Med.*, **24**, 147 (1926).

[332] Cantarow, A., *et al.*, *Endocrinology*, **21**, 368 (1937).

[333] *Cf.* among others, Greenwald, I., *Am. J. Physiol.*, **28**, 103 (1911); *J. Biol. Chem.*, **14**, 363 (1913); **61**, 649 (1924); **66**, 185, 217 (1925); **67**, 1 (1926); **82**, 531 (1929).

[334] McLean, F. C., *et al.*, *Am. J. Physiol.*, **113**, 141 (1935); **121**, 580 (1938).

[335] Marine, D., *J. Exp. Med.*, **19**, 89 (1914).

[336] Dragstedt, L. R., *Am. J. Physiol.*, **63**, 408 (1922); **64**, 424 (1929); **69**, 477 (1924); **77**, 296 (1926). Salvesen, H. A., *J. Biol. Chem.*, **56**, 443 (1923).

[337] Bergeim, O., *J. Biol. Chem.*, **70**, 35 (1926). Huffman, C. F., *et al.*, *Id.*, **84**, 257 (1929). Mitchell, H. H., *et al.*, *J. Nut.*, **14**, 435 (1937). Outhouse, J., *et al.*, *Id.*, **14**, 579 (1937); **15**, 257 (1938); **20**, 467 (1940). Cowgill, G. R., and French, R. B., *Id.*, **14**, 383 (1937). Hart, E. B., *et al.*, *J. Biol. Chem.*, **98**, 121 (1932).

[338] Loeb, J., *Am. J. Physiol.*, **3**, 383 (1900); **5**, 362 (1901); *J. Biol. Chem.*, **23**, 423 (1915).

[339] Macleod, J. J. R., "Carbohydrate metabolism and insulin", Longmans, 1926. "The fuel of life", Princeton Press 1928. Soskin, S., *Physiol. Rev.*, **21**, 140 (1941). Long, C. N. H., *Ann. Rev. Physiol.*, **4**, 465 (1942). Soskin, S., and Levine, R., *Biological Symposia*, **5**, 64 (1941).

As regards the carbohydrate-metabolism hormone insulin, we have first the discovery of the relation of the disease diabetes to an organic lesion of the pancreas; second, duplication of the disease by removal of the pancreas[339] (Mering and Minkowski, 1899); third, the correlation of the disease with special structures in the pancreas, the islets of Langerhans (Opie, 1901); fourth, the idea of the presence of a hormone (M.W. 35000, named "insulin" by Shaffer in 1916); fifth, the search for and discovery of the hormone. Several groups of workers independently prepared active extracts, but one[340] carried the work to the stage of successful substitution therapy in man.

There is likewise a parallelism between the regulatory effect of insulin on blood sugar and, for example, of parathormone on blood calcium. Bone is the bodily reservoir for blood calcium, and glycogen is the bodily reservoir for blood glucose (Sects. 10.4 and 10.5).

Insulin has at least three interrelated functions: (1) the homeostatic one (Sect. 10.4) of maintaining constant the glucose level in the blood by shifting the reaction glycogen $\rightleftharpoons$ glucose to the right or left; (2) storing glycogen in the liver and muscle; (3) catalyzing the oxidation of carbohydrate.

A more recent development is that the anterior lobe of the pituitary has an insulin-antagonizing hormone, the so-called diabetogenic or glycotropic factor[341]. Houssay[341] reported that an animal made diabetic by removal of the pancreas is improved with regard to diabetic symptoms (high sugar and ketone bodies in blood and urine) and lives longer if the anterior lobe of the pituitary is likewise removed. Such an animal (depancreatized and hypophysectomized) is called a "Houssay animal". It is, of course, very remarkable that an injury to two organs is more favorable than to one, and this fact emphasized dramatically the concept of balance. Young[342] confirmed the observations that hypophysectomy decreases diabetic intensity in diabetic animals, and he further observed that administration of A.P. extract to normal animals may lead to severe, permanent, diabetes. The effect is apparently by way of the islets of Langerhans, first overstimulated, than destroyed[343]. Diabetes may thus result from pituitary overactivity as well as from pancreatic underactivity.

It is important to note that removal of the adrenals in diabetic animals likewise improves the diabetic condition[344]. The adrenalectomy effect is observed only in the presence of the pituitary, indicating that the pituitary hormone acts through the intermediacy of the adrenals. This has been adequately confirmed.

The problem of endocrine balance and its relation to *ketosis* is so important in practice that it is desirable to outline it. First is the fact that in their metabolic history fatty acids apparently pass through a ketone stage, most conspicuously acetoacetic acid, $CH_3 \cdot CO \cdot CH_2 \cdot COOH$. But the "ketone bodies" also include beta-hydroxybutyric acid, $CH_3 \cdot CHOH \cdot CH_2 \cdot COOH$, and acetone, $CH_3 \cdot CO \cdot CH_3$. The overall reaction leading from, say, palmitin or palmitic acid to a ketone may be illustrated in several ways, for example, by the reaction

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[340] Banting, F. G., and Best, C. H., *J. Lab. Clin. Med.*, **7**, 251 (1922).

[341] Houssay, B. A., and Biasotti, A., *Endocrinology*, **15**, 511 (1931); *Arch. ges. Physiol.*, **227**, 239 (1931). See Thompson, D. L., *J. A. M. A.*, **115**, 2169 (1940).

[342] Young, F. G., *Endocrinology*, **26**, 345 (1940).

[343] Campbell, J., and Best, C. H., *Lancet*, **1**, 1444 (1938).

[344] Long, C. N. H., and Lukens, F. D. W., *J. Exp. Med.*, **63**, 465 (1936).

$$\underset{\textit{palmitic acid}}{C_{16}H_{32}O_2} + 19O_2 \longrightarrow \underset{\textit{acetoacetic acid}}{CH_3 \cdot CO \cdot CH_2 \cdot COOH} + 12CO_2 + 13H_2O$$

The accumulation of ketone bodies in diabetes used to be explained[345] by assuming that their oxidation involved a coupling with carbohydrate, that one molecule of glucose is needed to burn "smokelessly" one to two molecules of fatty acid, and that ketone bodies form in the absence of sufficient glucose.

The current idea seems to be[346] that carbohydrates are not antiketogenic in Shaffer's coupled-reaction sense but, more simply, in the sense that when the carbohydrate oxidation is low, fat oxidation is correspondingly high, and relatively high fat metabolism necessarily involves relatively high ketone formation. The fat metabolism is high when carbohydrate cannot be utilized, as in diabetes, during starvation (either total or specific carbohydrate starvation), when oxidation is confined to fat, following the administration of anterior pituitary "diabetogenic hormone"[347]. This is assumed to mobilize fat from the fat depots, causing hyperlipemia and fatty infiltration of the liver, which liver fat replaces the liver glycogen (the effects of both insulin and the pituitary diabetogenic hormone are on the liver—neither is effective in liverless animals[348]), and the metabolism is largely of fats. Insulin and available carbohydrate prevent ketosis by inhibiting fat infiltration into the liver and storing glycogen instead; the anterior diabetogenic factor, on the contrary, stimulates hyperlipemea and fat infiltration into the liver, with consequent high fat metabolism and therefore ketosis. It is possible that low blood sugar, or low dietary carbohydrate, stimulates the pituitary to produce the diabetogenic factor.

Ketosis is of considerable agricultural importance. Ketosis, like a certain type of milk fever caused by low blood sugar[349] (as well as by low blood calcium, discussed in the parathyroid section), is fairly common in high-producing ruminants in late winter and early spring[350]. The explanation may be, roughly, as follows[351]: (1) the soluble carbohydrates have been fermented and leached from the hay and silage by late winter and early spring; (2) great quantities of fatty acids are formed by fermentation in the rumen[352], especially if the fodder is low in soluble carbohydrate, and absorbed; (3) lactation (and gestation) makes great demands on the soluble carbohydrates. The result of the low glycogen reserve is high fat reserve in the liver with ketone formation as explained above. The remedy is, obviously, feeding good roughage (containing high levels of soluble carbohydrate) and, if necessary, such feeds as molasses, up to two pounds a day (to lactating dairy cows).

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[345] Shaffer, P. A., "Ketogenic-antiketogenic balance", *J. Biol. Chem.*, **47**, 449; **49**, 143 (1921); **54**, 399 (1922).

[346] Soskin, S., and Levine, R., *Biological Symposia*, **5**, 64 (1941). MacKay, E. M., "Ketosis", *J. Clin. Endocr.*, **3**, 101 (1943).

[347] Long, C. N. H., *Cold Spring Harbor Symposia on Quantitative Biology*, **5**, 344 (1937). A full review is presented on the possible existence of ketonuria-producing hormones in the A.P. distinct form carbohydrate-metabolism hormones and of other diabetogenic hormones. See also Russell, Jane A., "Relation of anterior pituitary to C. H. metabolism", *Physiol. Rev.*, **18**, 1 (1938).

[348] Mirsky, I. A., *Am. J. Physiol.*, **115**, 424; **116**, 322 (1936).

[349] Little, W. E., and Wright, N. C., "Milk fever", *Brit. J. Exp. Path.*, **6**, 219 (1925). Nicholson, J. A., and Shearer, G. D., "Lactation tetany", *Vet. J. (Ireland)*, **44**, 388 (1938).

Duncan, Huffman and Tobin reported that the acetone-body concentration in their cows suffering from ketosis was 23 mg per cent in the blood and 155 mg per cent in the urine. Following recovery, the concentration was, respectively, 3 and 54 mg per cent in the blood and urine. Manifestations of ketosis in cattle (depression or excitement, decline in milk production and feed consumption, depraved appetite, stiffness) are said to begin when the ketone bodies exceed, respectively, 10 and 20 mg per cent in the blood and urine.

Summarizing, this section presents a diagrammatic outline of one aspect of the hormonal regulation of carbohydrate and fat (ketosis) metabolism, with notes on their relation to the nature of the food supply. Other neuro-endocrine factors influencing metabolism were discussed in the thyroid and adrenal sections. Non-hormonal catalysts, including choline, influencing especially fat metabolism, are discussed in Chapters 6 and 20.

7.7: Anterior-pituitary and growth hormones. The removal of the anterior-pituitary (A.P.) in growing animals not only stops growth but leads to marked loss in body weight[353]. Growth is resumed at the normal or even at supernormal levels on *injecting* (but *not ingesting*, except possibly in some amphibians) A.P. extract[354], or simply by daily implantation of pituitary tissue[355].

On the other hand, A.P. injection or implantation into normal animals leads in young animals to gigantism[354, 356] and in some species of adult animals

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[350] Sjollema, B., "Metabolic cattle disorders", *Nut. Abst. Rev.*, **1**, 621 (1932).

[351] Duncan, C. W., Huffman, C. F., and Tobin, H. A., *J. Am. Vet. Med. Assn.*, **95**, 690 (1939). Boddie, G. F., *Vet. Rec.*, **15**, 1539 (1935). Fincher, M. G., *Cornell Vet.*, **26**, 143 (1936).

[352] Washburn, L. E., and Brody, S., Univ. Missouri Agr. Exp. Sta. Res. Bull. 263, 1937.

[353] Cushing, H., "The pituitary body and its disorders", Philadelphia, 1912.

[354] Evans, H. M., and Long, J. A., *Anat. Rec.*, **21**, 62 (1921); **23**, 19 (1922); also *Proc. Nat. Acad. Sci.*, **8**, 38 (1922). Evans, *Harvey Lectures*, **19**, 212 (1924); Evans, Meyer, K., and Simpson, M. E., *Memoirs Univ. Calif.* (1933). Evans, *et al.*, *Endocrinology*, **27**, 605 (1940); *Am. J. Physiol.*, **135**, 614 (1942), and numerous papers since 1921.

[355] Smith, P. E., *Anat. Rec.*, **25**, 150 (1923); *J. A. M. A.*, **88**, 158 (1927); *Am. J. Anat.*, **45**, 205 (1930). See also Thompson, K., and Gaiser, D. W., *Yale J. Biol. Med.*, **4**, 677 (1932).

[356] Putnam, T. S., Benedict, E. B., and Teel, H. M., *J. Physiol.*, **84**, 157 (1928); *Arch. Surg.*, **18**, 1708 (1929). Teel and Cushing, *Endocrinology*, **14**, 157 (1928). Evans, Meyer, and Simpson[354].

(dogs, but not rats) to acromegaly. In both there is marked visceromegaly[356], increased size of chest, thickening of skin and increased hair growth. The effects on different organs varies with the species. Splanchomegaly has been noted in acromegatic humans and dogs and splanchomicria in pituitary dwarfism. The spleen is hypertrophied to double the normal size due to hyperplasia of the reticular and endothelial cells of the red pulp[357] and hypertrophy of the liver by true hyperplasia[358].

The female rats administered pituitary growth hormone by Evans attained 700 grams as compared to 300-gram litter mates; and male rats reached 900 grams compared to 450-gram litter mates. The successive growth increments in the rats decreased with successive hormone increments until further hormone additions were without effect. Forces other than epiphyseal closure operate to limit growth.

This upper limit may, perhaps, be reached without hormone administration by dietary means alone. Thus the Anderson-Smith fed rats[359] weighed 300 grams at 63 days, more than the hormone-treated rats of Evans and Long[360] that weighed 228 grams at 75 days. The Anderson-Smith fed rats weighed 500 grams at 123 days, close to the hormone-treated rats of Evans and Simpson[361] that weighed 500 grams at 125 days. There may, however, have been genetic size differences between the Evans and the Anderson-Smith rats, so that these two groups of rats may not have been comparable.

There is a large literature on pituitary gigantism associated with pituitary tumors[362], and on dwarfism associated with defective pituitary inheritance[363] or hypophysectomy[364].

These observations indicate that the pituitary has a major function in growth and development. One problem at present under investigation is whether this pituitary control is (1) *direct* on the growing tissue, by means of specific growth or somatotropic hormone(s), or (2) *indirect* by way of pituitary trophic or tropic hormones, which act as "triggers" on other "target" endocrines, exemplified by action of the pituitary thyrotropic hormone on the thyroid, which in turn controls growth aspects (Fig. 7.3). It is evidently a difficult, if not impossible, task to separate these two different types of controls.

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[357] Perla, D., *J. Exp. Med.*, **63**, 599 (1936).

[358] Brues, A. M., *et al.*, *Arch. Path.*, **22**, 658 (1936).

[359] Anderson, W. E., and Smith, A. H., *Am. J. Physiol.*, **100**, 511 (1932).

[360] Evans, H. M., and Long, J. A., *Anat. Rec.*, **21**, 62 (1921); **23**, 19 (1922).

[361] Evans, H. M., and Simpson, *Am. J. Physiol.*, **98**, 511 (1931).

[362] Marie, P., *Rev. de Med. (Paris)*, **6**, 297 (1886); *Arch. Med. Exper. Anat. Path.*, **3**, 539 (1891). Cushing, H., "The pituitary body and its disorders", Lippincott, 1912. Cushing, H., and Davidoff, L. M., "Acromegaly", Monograph of the Rockefeller Institute, No. 22, 1927. Cushing, *Harvey Lectures*, **28**, 90 (1932-33). Weinberg, S. J., "Gigantism", *Ann. Med. Hist.*, **3**, 650 (1931).

[363] Bayer, L. M., and Gray, H., "Growth of pituitary dwarfs", *Intern. Clinics*, **3**, 15 (1937). Engelbach, W., "Endocrine Medicine", Thomas, 1932; *Endocrinology*, **17**, 280 (1933); **18**, 387 (1937). Schaeffer, R. L., *Id.*, **20**, 64 (1936).

[364] Smith, P. E., *J. A. M. A.*, **88**, 158 (1927); *Am. J. Anat.*, **45**, 205 (1930). Aschner, B., *Wien. Klin. Wchnschr.*, **22**, 1730 (1909); *Arch. ges. Physiol.*, **146**, 1 (1912). Richter, C. P., and Wislocki, G. B., *Am. J. Physiol.*, **95**, 481 (1930). Thompson, K., and Gaiser, D. W., *Yale J. Biol. Med.*, **4**, 677 (1932). Evans, H. M., *et al.*, *Univ. Cal. Memoir* **11**, 1933. Lee, M., and Ayres, G. B., *Endocr.*, **20**, 489 (1936). Parkes, A. S., and Rowlands, I. W., *Proc. Roy. Soc.*, **125B**, 214 (1938).

The following recent data[365] on the growth of a human giant are instructive on what a pituitary abnormality may lead to. The parents, brothers, and sisters were normal (Fig. 7.6).

Age (years)	Weight (lbs)	Height (feet) (inches)
Birth	$8\frac{1}{2}$	
$\frac{1}{2}$	30	
9	178	6–0
11		6–7
14		7–5
19	435	8–6
21[366]	495	8–8
22	491	$8\text{–}9\frac{1}{2}$
(died from infection of foot)		

The literature reports taller men (cf. Biblical 9 ft 9 in for Goliath, 9 ft 9 in for an Arabian giant reported by the Roman Pliny, etc.), but Dr. Humbred believes that this man, less than 9 feet, is the tallest on record, representing the genetic ceiling.

Though large, these giants are weak. Thus injection of A.P.E. enlarges the liver, but the enlargement is often associated with a central atrophy or necrosis[367]. Similar results of external enlargement and internal degeneration were reported on bone growth in guinea pigs and mice[368].

The medical literature is concerned with the use of growth-hormone preparations on various types of dwarfs. Dwarfism is commonly divided into: (1) anterior hypopituitarism; (2) primary anterior pituitary and secondary thyroid deficiency; (3) primary thyroid and secondary anterior pituitary deficiency. Uncomplicated hypopituitarism (normal except hypofunction of the eosinophil cells) is associated with small size but normal proportions; hypothyroidism is associated with abnormal bodily proportions and maldifferentiation. The thyroid and pituitary—as well as many other endocrines—act synergistically. The therapeutic hormone preparation necessarily varies with the cause and nature of the dwarfism. The pituitary dwarf, whose bodily proportions, texture of skin and hair, and mental development are normal, although often sexually undeveloped, is treated with the "pituitary growth" preparation. The thyroid dwarf, whose bodily proportions, texture of skin and hair and mental development are abnormal, is treated with thyroid. Because of the synergistic interrelations of pituitary and thyroid hormone, both are often employed together. Certain types of bone-growth dwarfisms may be associated with defective adrenals. It has been reported[369] (but not confirmed) that adrenalectomy results in a stunting of bone growth similar to that of hypophysectomy. Whichever the mechanism of action of the pituitary on growth, it is undoubtedly indispensable during postnatal growth and development.

But in early prenatal life, prior to the development of the functional pituitary and the other endocrines[370], the chick embryo for example, seems to be doing well enough without the pituitary and at ages when growth and development are most rapid. Does the egg contain all the hormones? Are these growth-development catalysts needed in later life only to overcome some back pressure, some "resistance"; or are the hormones needed to "detoxify" something that develops with increasing age?

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[365] Humberd, C. D., *J. A. M. A.*, **108**, 544 (1937). See also Gray, H., "The Minneapolis Giant", *Annals. Intern. Med.*, 10, 1669 (1937). For the older literature, see Silberberg, M. and R., *Arch. Path.*, **36**, 512 (1943).

[366] *Time Magazine*, March 20, 1939, p. 57.

[367] Putnam, Benedict, and Teel[356]. Downs, W. G., *J. Dent. Res.*, **10**, 601 (1930).

[368] Silberberg, M. and R., *Endocrinology*, **29**, 475 (1941); also *Am. J. Path.*, **15**, 547 (1939); **16**, 491, 505; **17**, 189 (1940).

[369] Ingalls, T. H., and Hayes, D. R., *Endocr.*, **29**, 720 (1941).

Primitive organisms do not have this elaborate net-work of endocrines. Indeed, it is said that early removal of the anterior pituitary in so highly evolved an organism as the oxolotl salamander does not interfere with growth[371]. Time, and stage of maturity, both individual and racial, seem to be decisive factors in the production and action of endocrines[372]. Increasing involvment of ever more complex integrating devices—neuro-endocrine systems—is a conspicuous feature of organic evolution, both individual and racial. Simple cell division under simple nutritive conditions does not appear to require a pituitary or other endocrine.

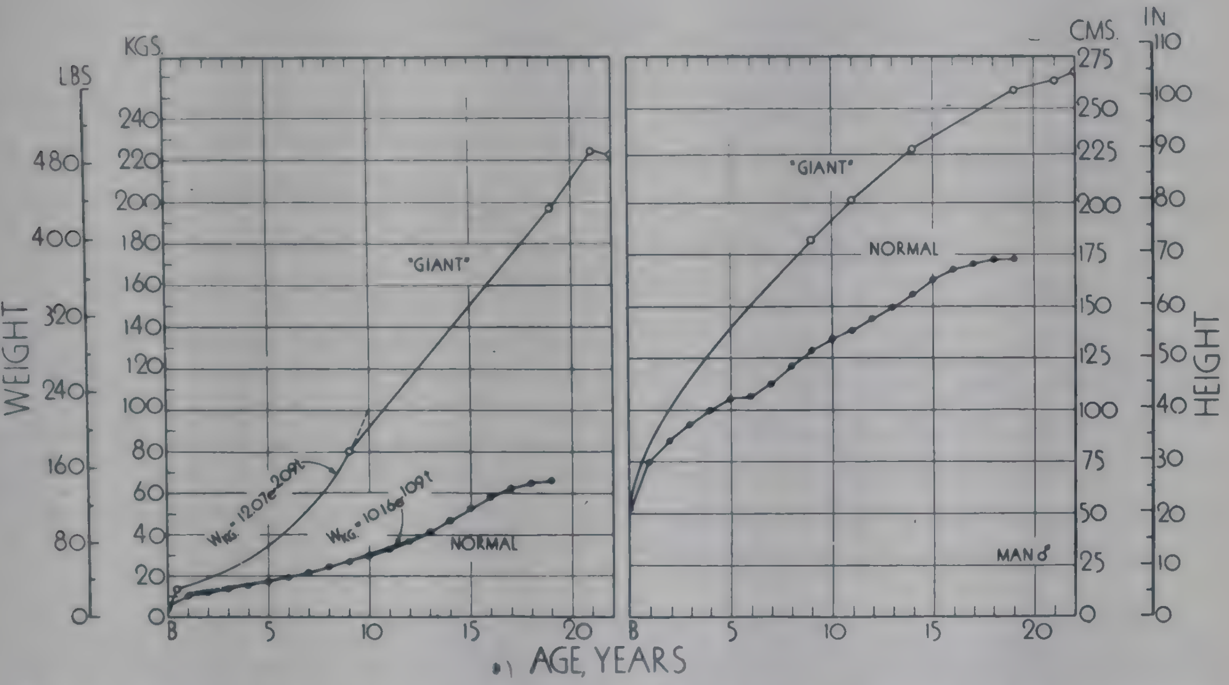

Fig. 7.6—Comparative growth of normal and giant boys. The values of the exponent in the equation indicates the relative (or percentage when multiplied by 100) growth rates. Thus prior to age 9 or 10 years the giant grew at 20.9% while the normal boy grew at 10.9% per year (for elucidation of growth rate see Ch. 16).

The investigational difficulties are complicated by racial as well as species differences. Thus different dove races vary in their thyroid size[373] and in pituitary lactogenic hormone (prolactin) concentration[374]. Differences in lactogenic hormone concentration were also observed between beef and dairy cattle[375], goats[376], rats[377], mice[378], and dogs[379, 380] at various ages and periods of gestation and lactation (lactogenic hormone per mg pituitary is about 0.01 I.U. in non-lactating and about 0.05 I.U. in lactating mice, rats, and rabbits).

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[370] *Cf.* Collip, J. B., *et al.*, *Nature*, **131,** 56 (1933). Tugo, N. W., *J. Exp. Zool.*, **85,** 271 (1940).

[371] Burns, R. K., and Buyse, A., *Anat. Rec.*, **51,** 333 (1932).

[372] Riddle, O., *Cold Spring Harbor Symposia on Quantitative Biology*, **10,** 7 (1942). Martindale, F. M., *Anat. Rec.*, **79,** 373 (1941) (thyrotropic hormones in the chick first found on the tenth day). Rankin, R. M., *Id.*, **80,** 123 (1941) (thyroxine secretion in fetal pig begins at 52 days).

[373] Riddle, O., *Am. Naturalist*, **68,** 385 (1929).

[374] Riddle, *et al.*, *Am. J. Physiol.*, **125,** 722 (1939).

[375] Reece, R. P., and Turner, C. W., Univ. Missouri Agr. Exp. Sta. Res. Bull. 266, 1937.

[376] Koger, M., Meites, J., and Turner, C. W. (unpublished, 1943).

[377] Reece, R. P., Hathaway, I. L., and Davis, H. P., *J. Dairy Sci.*, **22,** 1 (1939).

[378] Hurst, V., and Turner, C. W., *Endocrinology*, **31,** 334 (1942).

The analytic difficulties are further multiplied by differences in interrelations and synergisms in different species. Thus the thyrotropic and lactogenic hormones are synergistic and mutually supplementary in their effects on growth in dwarf mice[381] and in heat production in pigeons[382], and so on.

The above discussion does not answer the question as to whether or not there is anterior-pituitary hormone acting *directly* on body growth (independently of other target glands), as is believed by Evans. General agreement will probably be delayed until (1) the pure A.P. growth hormone (if such is present) is obtained, and (2) it is demonstrated that it does not act on other endocrines, or that it stimulates growth in the absence of other endocrines or hormones—perhaps an impossible demonstration since growth is an overall process, the resultant of innumerable interrelated factors. It therefore seems most logical to assume that growth is a function of many hormones, not of one specific growth hormone.

The most interesting agricultural feature of the claimed effect of A.P. "growth hormone" injection in young animals is the increase in growth rate and ultimate body size in general and protein retention in particular. The ultimate body size following A.P. "growth hormone" injection is apparently not larger than can be obtained by proper dietary means[383]. The important claim, somewhat difficult to accept, is that on a *given* quantity of the same food (when the animals are said to be "pair fed", see Ch. 20) animals treated with A.P. extract grow faster in weight[384].

Lee[384] reported data on four groups of rats: (1) one was analyzed at the beginning of the experiment; (2) another served as control; (3) a third was treated daily with 3 rat units of pituitary growth extract, and was restricted in food consumption to the same amount as that voluntarily eaten by its control mate; (4) a fourth was likewise treated with growth extract but was allowed food *ad libitum*.

Lee's data indicate that (A) the treated animals on the *ad libitum* diet consumed 10 to 15 per cent more food than the non-treated controls; (B) the treated animals gained more weight than the untreated even if pair-fed (consuming the same amount of feed as the controls); (C) the heat production per unit area was the same in the treated and non-treated animals. The apparent conclusion is that growth hormone not only in-

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[379] Stockard, C. R., "The physical basis of personality", New York, 1931, and "The genetic and endocrinic bases for differences in form and behavior", Philadelphia (Wistar Institute), 1941.

[380] Evans, H. M., *et al.*, *Memoir Univ. Calif.*, **11** (1933).

[381] Bates, R. W., Laanes, T., McDowell, E. C., and Riddle, O., *Endocrinology*, **31,** 53 (1942).

[382] Riddle, *et al.*, *Id.*, **20,** 1 (1936).

[383] Bryan, A. H., and Gaiser, D. W., *Am. J. Physiol.*, **99,** 379 (1932). Anderson, W. E., and Smith, A. H., *Id.*, **100,** 511 (1932).

[384] Lee, M. O., *Proc. Assn. Res. Nerv. Mental Dis.*, **17,** 193 (1936), based on: Lee and Schafer, N. K., *J. Nut.*, **7,** 337 (1934); *J. Biol. Chem.*, **108,** 355 (1935). Lee and Ayres, G. B., *Endocrinology*, **20,** 489 (1936). Marx, W., *et al.*, *Am. J. Physiol.*, **135,** 614 (1942).

creases food consumption, but also increases weight gains, even if the food consumption is not increased.

Lee's results, illustrated by Fig. 7.7a, b seem puzzling, because the hormone-injected rats gained more weight than the controls in spite of the fact that (a) they consumed no more food than the controls; (b) they must have had a higher maintenance expense than the controls because they were larger; (c) they probably had a higher maintenance expense because, being restricted to the food intake of the smaller animals, they were probably hungrier and more restless.

How should one explain in the face of the second law of thermodynamics (Ch. 2) the greater weight gain of the hormone-treated animals on the same energy intake as the controls? One possibility is that the differences in weight gain are due mostly to differences in water, with proportionally greater protein and mineral storage (the caloric value of 1 g of fat gain is equivalent to 8 g of non-fat gain). This idea that the weight gain represents not energy but largely water is substantiated by the following tabulation (last column by the writer) of Lee's data.

	Gain in empty carcass, weight (g)	Gains in empty carcass (g) in the form of:				Estimated Cal in carcass, assuming 5.7 Cal/g protein and 9.4 Cal/g fat
		Water	Fat	Protein	Ash	
12 controls	716	324	281	96	22.7	3189
12 treated	1217	771	162	237	45.1	2874

The *stored energy in the treated rats is seen to be less than in the untreated smaller rats.* The larger size of the treated animals is due mostly (about 90 per cent) to water gain, with corresponding gain in protein and ash (ratio water to protein is about 3.3 in both groups; ratio of water to ash is about 14 in the control and about 17 in the treated animals). This result is somewhat similar to that on growth-acceleration of mice by thyroid administration; the gains were due not to total energy but to extra water, protein, and mineral storage.

Lee interpreted the greater water, protein, and ash content of the treated rats as due to their chemical immaturity[385] in the sense that "the increment of body material during active growth is itself also characterized by a relatively high content of water, protein, and salts and low content of fat". Lee also investigated the changes in body weight and body composition of normal and hypophysectomized rats pair-fed 33 days (Fig. 7.8B). In spite of the same energy consumption, the hypophysectomized rats lost weight much more rapidly than the controls.

This impermanency of the gains in the A.P.-injected animal was termed by Lee "lability of growth effect", and is interpreted by him as due to storage of the labile "deposit protein"[386]. "In some cases . . . control animals overtake and pass their erstwhile treated mates". Lee's interpretation that A.P. growth-hormone injection accelerates true growth is substantiated by Brues'[387] data on more rapid liver regeneration after partial hepatectomy in hormone-injected than in (pair-fed) control rats. The increase in size was due to true hyperplasia[388] of all liver components in the same proportions as they existed initially. The liver in the injected rats contained more water, ash, and protein than in the control rats. All visceral organs grew more rapidly

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[385] Moulton, C. R., *J. Biol. Chem.*, **57**, 79 (1923). The mammalian embryo contains 70 to 100 times as much water as nitrogen; the mature animal contains about 20 times as much water as nitrogen.

[386] Rubner, M., *Arch. Hyg.*, **66**, 45 (1908).

[387] Brues, A. M., *et al.*, *Arch. Path.*, **22**, 658 (1936).

[388] Lee, M., and Freeman, W., *Endocrinology*, **26**, 493 (1940).

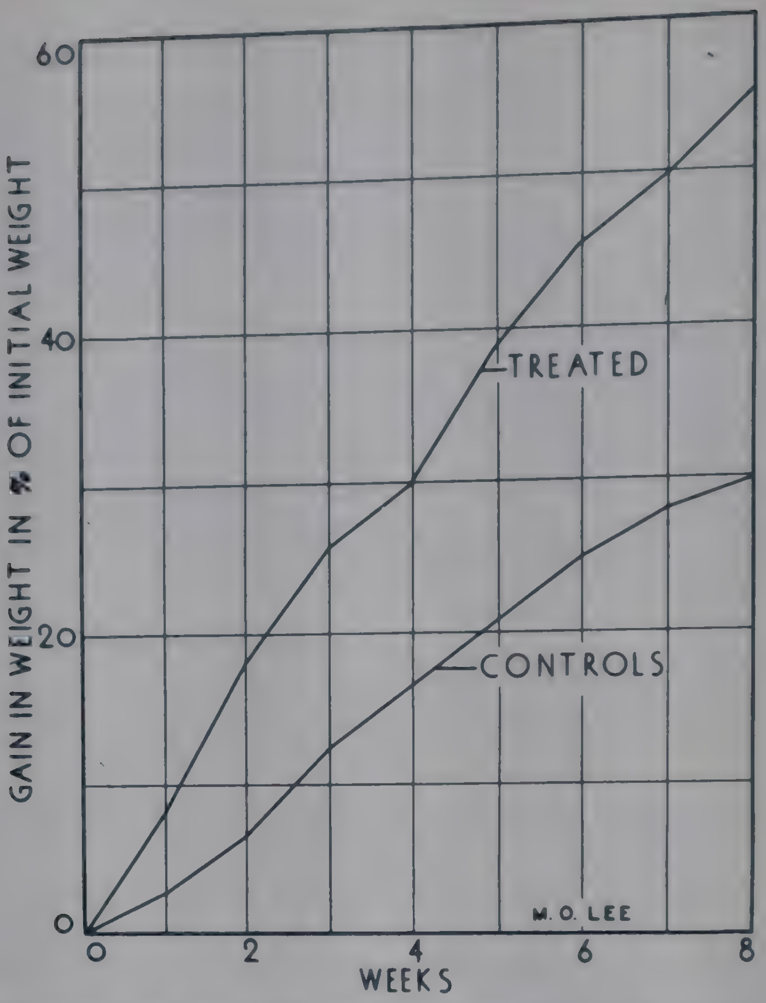

Fig. 7.7a—Growth of Lee's pair-fed rats, controls, and pituitary-treated.

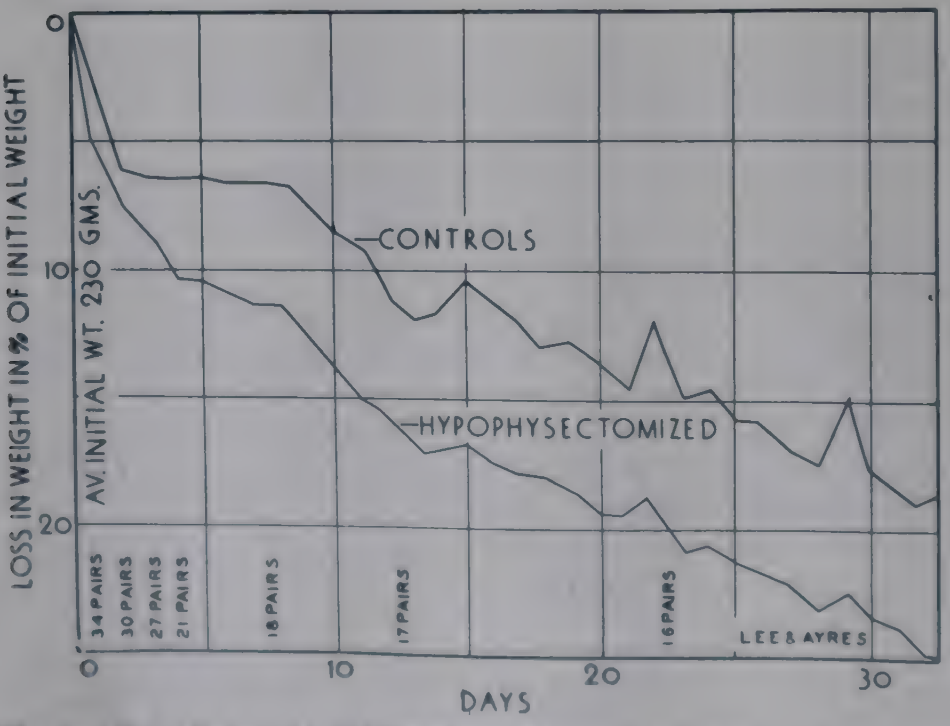

Fig. 7.7b—Changes in body weight of Lee's pair-fed control and hypophysectomized rats.

following hormone injection than the body as a whole. Thus in dogs made acromegalic by A. P. growth extracts, the ratio $\frac{\text{weight hormone-treated animals}}{\text{weight control animals}}$ was reported[389] to be 1.87 for the body as a whole; 2.2, heart; 3.36, lungs; 3.42, liver; 1.16, spleen; 2.67, pancreas; 2.43 kidneys. The glomeruli and tubules of the kidneys were greatly enlarged, and subcutaneous and omental fat decreased.

The A. P. Growth extract stimulates the activity of the periosteal ossification zones[390] without the benefit of increased phosphatase activity[391]. However, as previously noted, the larger size may be associated with internal degeneration.

Summarizing, the anterior-pituitary occupies the highest position in the endocrine order of growth regulators. However, the pituitary does not seem to be essential in early embryonic growth, and it may even be removed in some lower forms, for example, amphibian larvae, without inhibiting growth. Moreover, growth continues for a considerable time even after the pituitary is removed. At later ages, however, the pituitary appears to be indispensable for growth and even for maintenance of mammals. This result is not surprising since, as explained in Sect. 7.1, removal of the pituitary leads to atrophy of many of the major endocrines, such as thyroids, adrenals, islets of Langerhans, and others, thus interfering with the anabolic processes. Growth and maintenance could not occur without some of the major internal metabolic catalysts.

There is no agreement on the answer to the question concerning the presence of a special somatotropic hormone independent of the other pituitary tropic hormones. The evidence favoring Evans' theory is that certain A.P. preparations injected at a proper age in susceptible animals induce gigantism in young animals (rats at any rate) and acromegaly in mature animals (some breeds of dogs at any rate), resembling the corresponding states in man suffering from certain types of pituitary tumor.

One of the outstanding effects in the production of gigantism is delay in epiphysial closure and stimulation of epiphysial cartilage[392]; hence the alternate name, chondrotropic hormone, for this pituitary growth factor(s).

The beneficial effects of pituitary administration to dwarfs is not proof of the presence of a special growth hormone, since crude pituitary contains tropic hormones for other growth-promoting glands which the dwarf may lack. Thus one pituitary dwarf began to grow after insulin therapy[393], indicating that insulin (its production is also under A.P. control) has growth-promoting properties aside from its effect on carbohydrate metabolism. Similarly, adrenalectomy prevents bone growth[394], and so adrenal deficiency may be corrected by A.P. administration, as A.P. contains an adrenotropic hormone.

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[389] Putnam, Benedict, and Teel[356] (1929).

[390] Handelsmann, M. B., and Gordon, M. B., *J. Pharmacol. Exper. Therap.*, **38**, 349 (1930).

[391] Wilkins, W. E., *et al.*, *Am. J. Physiol.*, **112**, 477 (1935).

[392] Ross, E. S., and McLean, F. C., *Endocrinology*, **27**, 329 (1940).

[393] Beck, H. G., and Suter, G. M., *Id.*, **22**, 115 (1938).

[394] Ingalls, T. H., and Hayes, D. R., *Id.*, **29**, 720 (1941).

7.8: Notes on miscellaneous hormones

7.8.1: Hormones in evolution. The function of a given hormone may vary in different organisms, at different evolutionary levels. Thus in lower organisms, there are substances—such as estrin in insects, adrenaline in worms, oxytocic principle in fishes, progesterone in beans—which appear to be useless to them but which serve as hormones in more evolved organisms[395]. Moreover, a given hormone may act on different tissues in different species. Thus, lactogenic hormone stimulates the mammary gland to secrete milk, and the pigeon's crop gland to proliferate and to secrete "pigeon milk". The testicular hormone is required for the growth of antlers in the red deer, but not in the reindeer[396]. The ovarian hormone is necessary for sexual dimorphism of feathers in the fowl, but not in the sparrow, where it is controlled by the chromosomes of the epidermal cells[397].

Keith[398] in England and Stockard[399] in the United States discussed the problem of hormones in evolution[400]. On the basis of his data Stockard concluded that breed characteristics of dogs are apparently due to endocrine peculiarities, and that these are transmitted in Mendelian manner.

Such characteristics as maleness, femaleness, broodiness[401], aggressiveness, and similar emotional patterns, or psychic states, so important in evolution, seem to reflect neuro-endocrine patterns. Indeed, the broodiness (maternal drive or maternal instinct in birds) may be measured quantitatively by the amount of prolactin in their pituitaries[402], and the potential genetic reproductive ability of domestic fowl may perhaps be measured by the quantitative response (increase in weight) of the gonads, thyroids, and combs on the administration of a given dose of anterior pituitary (gonadotropic and thyrotropic) extract[403].

7.8.2: Endocrines in embryogenesis[404]. Embryonic growth and development are said to be stimulated by "hormones" named *evocators*, particularly involved in the quantitative aspects of growth, and *individuators* or *organizers*, especially in developmental coordination, differentiation, and morphogenesis (Ch. 17).

In the egg stage, the individual exists in a potential form of extraordinary plasticity. The egg may divide to give rise to several individuals. Human identical (monozygotic) twins result from complete division of a single cell (Siamese twins from incomplete divion). The eggs of the Texas armadillo regularly divide into four parts, giving rise to our young. In some parasitic insects one egg often forms as many as 2000 separate mbryos[405]. Spemann and others produced "secondary embryos" by "induction". But this plasticity rapidly declines with differentiation.

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[395] Collip, J. B., *Sci. Monthly* (Nov., 1936); Thompson, D. L., *Nature*, **80**, 543 (1932).

[396] However, the antler in the red deer is anatomically distinct from the antler in the reindeer.

[397] Danforth, C. H., "Relation of genetic and endocrine factors in sex", Ch. 6 in Sex and Internal Secretions (Ed. E. Allen), 1939.

[398] Keith, A., "The evolution of human races in the light of the hormone theory", *Bull. Johns Hopkins Hosp.*, **33**, 155, 195 (1922); *Nature* (Aug. 18, 1923).

[399] Stockard, C. R., "Human types and growth reactions", *Am. J. Anat.*, **31**, 261 (1923). "The physical basis of personality", New York, 1931. Also, *Am. Anatomical Memoirs*, No. 19, Wistar Institute, Philadelphia, 1941.

[400] See also, Zuckerman, S., *Man*, **36**, 129 (1936).

[401] Riddle, O., *Cold Spring Harbor Symposia on Quantitative Biology*, **5**, 218 (1937); **10**, 12 (1942); *Sci. Monthly* (Aug. 1938).

[402] Byerly, T. C., and Burrows, W. H., *Proc. Soc. Exp. Biol. Med.*, **34**, 844 (1936).

[403] Munro, S. S., *et al.*, *Am. Naturalist*, **77**, 256 (1943).

[404] Needham, J., *Proc. Roy. Soc. Med.*, p. 1577 (1936). Spemann, H., "Embryonic development and induction", New Haven, 1938; *Brit. J. Exp. Biol.*, **2**, (1925). Barth, L. G., and Graff, S., *Cold Spring Harbor Symposia on Quantitative Biology*, **6**, (1938). Waddington, C. H., *Proc. Roy. Soc.*, **125B** (1938). Needham, First *Growth* supplement (1939) p. 45. Waddington, *Id.*, p. 37. Needham, J., "Biochemistry and morphogenesis", Macmillan, 1942.

Spemann[404] began his research to determine whether the causes of embryonic differentiation are chiefly intrinsic or extrinsic. He cut in two, in various planes, eggs and early embryos of newts. Prior to the gastrula stage, a whole embryo of half-size developed from each half of the egg, provided the cutting was in the median plane. Following the gastrula stage, when "labile determination" becomes "final", cutting of the gastrula results in abnormalities, and determination of the embryonic parts seemed to be fixed. The above discussion indicates that the destinies of the parts of the embryo are not fixed at the beginning, but become so only as development proceeds. These early potentialities rapidly disappear; each part acquires definite destinies which cannot be altered by experimental procedure. Spemann demonstrated the presence of growth *organizers* of various grades. He found that the *head organizer* would induce heads either in head or tail region (individuation), and that *tail organizers* would produce heads in the head region and tails in the tail region (evocation). The *competence*, the response of the receptor tissues to the organizer, to form head or tail is determined by the age of the tissues as well as by the organizer. Thus at first gill-forming competence is present over all the surface of the neurula, but later it is found only in the gill area.

The chemical nature of the evocator is indicated by the fact that it is not destroyed by boiling[406]. Coagulated dead pieces of dorsal lip induce secondary neural axes just as when living. Amphibian eggs coagulated by heat can produce new eyes and lenses when implanted[407]. Cell-free extracts from neurulae induce neural tubes when implanted in other embryos[408].

The organizers are found at all ages. The adult mammalian liver is rich in them[409]. In other words, the decisive factor is not the presence of the "hormone", but the presence of the *competence* in the tissue to be affected by it. The concept of hormone and tissue-competence, or trigger-target, relation is true for all hormones and tissues at all ages. Thus the lactogenic hormone stimulates only the pigeon crop to grow and the mammary gland to secrete milk; estrogens stimulate only female genital tissue to grow and androgens stimulate male sex tissue. The organizers, like sex hormones, cortical sterides, and vitamin D, appear to contain the cholesterol ring (Fig. 7.1).

Cancerous growths and teratomata may be due to the presence of uncontrolled evocators or growth hormones, and also to the escape of tissues from the influence of the "individuation field" (Ch. 10).

The growth evocators may be suppressed by dietary factors. Thus a sow receiving a ration deficient in vitamin A may farrow pigs devoid of eye-balls[410] or limbs[411]. These defects may be expressions of faulty interrelations between vitamin, hormone, and target tissue (see, however, Sects. 7.3.2 and 20.2).

In closing, one is tempted to mention the spectacular reports on the growth-accelerating effects of thymus extract[412] (in the tenth generation the rats matured in about one-fifth the usual time) and growth-retarding effects of a pineal extract[413]. These have not yet been confirmed[414].

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[405] Patterson, J. T., *Quart. Rev. Biol.*, **2,** 393 (1927).

[406] Waddington, C. H., *Phil. Trans. Roy. Soc.*, **221B,** 179 (1932); *J. Exper. Biol.*, **13,** 75, 86 (1936). Holtfreter, J., *Arch. Entwicklm*, **128,** 584 (1933).

[407] Lopaschov., G., *Nature*, **136,** 835 (1935). Needham, *et al.*, *Proc. Roy. Soc.*, **114B,** 393 (1934); Spemann, *et al.*, *Naturwiss.*, **21,** 505 (1933).

[408] Waddington and Walsky, A., *J. Exp. Biol.*, **13,** 92 (1936).

[409] Needham, Waddington, and Needham, *Proc. Roy. Soc.*, **114B,** 393 (1934); **117,** 289 (1936). Witschi, B., *Proc. Soc. Exper. Biol. Med.*, **27,** 475 (1930); **31,** 419 (1934); *Arch. Entwicklm.*, **102,** 168 (1924). Bills, C. E., *Physiol. Rev.*, **15,** (1935).

[410] Hale, F., *J. Heredity*, **24,** 105 (1933). Moore, L. A., *J. Nut.*, **17,** 443 (1939).

[411] Zilva, S. S., Golding, J., Drummond, J. C., and Coward, K. H., *Biochem. J.*, **15,** 427 (1921).

The supposed growth-accelerating effects of the thymus extract were attributed to its glutathione, and similar results were said to have been obtained by injecting rats with glutathione[415]. There is a wide belief that glutathione stimulates cell proliferation[416] (see also Ch. 6). The problem appears to be confused and seems to have been dropped for the moment.

7.8.3: Notes on green-plant hormones[417]. As previously explained (Sect. 6.4.3), the members of the vitamin B complex of the animal nutritionist are identical with the members of the bios complex or the "growth factors" of the microbiologist. The self-sufficient green plants also need these factors, but green plants produce them internally, as animals produce hormones internally. Therefore, by definition (Sects. 6.1 and 7.1), these factors are vitamins (exogenous catalysts) to animals and hormones (endogenous catalysts) to the self-sufficient plants.

The plant hormones are produced not by endocrine glands (plants have none) but, perhaps, by the undifferentiated, rapidly growing embryonic tissues; formation of protoplasm and of hormones may be simultaneous in the same growth centers.

As is generally known, there is differentiation of functions between leaf, stem, and root; and looking back, it would seem natural to assume that some of the plant hormones might be produced in one part of the plant and not in another. This was indeed beautifully demonstrated as regards thiamine (vitamin B_1), pyridoxine (vitamin B_6), and nicotinic acid.

The demonstration, conducted by Robbins and associates at the University of Missouri, consisted in cultivating excised tomato-plant roots *in vitro* in a nutrient solution of sugar and salts, with and without vitamin supplements. These isolated roots did not grow on the basic sugar-salt solution, but did grow when supplemented with a crude yeast extract[418] and still better with whole yeast[419].

A search for the essential yeast constituents proved them to be thiamine[420] and pyridoxine[421]. A similar, independent investigation by Bonner[422] showed that excised pea roots need thiamine and nicotinic acid, and flax roots need only the thiamine supplement.

In addition to the vitamin type of plant hormone, there are others, the best known of which is auxin (auxin A and auxin B, or auxentriolic and auxenolonic acids).

The auxin was isolated (interestingly enough, from urine), structure determined, and named by Kögl[423]. Auxin A has the composition $C_{18}H_{32}O_5$ and contains three hydroxyl groups forming a lactone. Auxin B has the composition $C_{18}H_{30}O_4$, an isomeric B-keto acid of auxin A. There are also many "heteroauxins", laboratory products which show auxin effects on plants, the best known and most effective of which is indole-3-acetic acid, also first isolated (from urine) by Kögl[424].

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[412] Rowntree, L. G., *et al.*, *Endocrinology*, **20**, 342 (1936); **21**, 659 (1937); **22**, 335 (1938).

[413] Rowntree, *et al.*, *J. A. M. A.*, **105**, 592 (1935). *Ann. Int. Med.*, **9**, 359 (1935); *Endocrinology*, **20**, 348 (1936).

[414] Segaloff, A., and Nelson, W. O., *Am. J. Physiol.*, **130**, 67 (1940); *Endocrinology*. **27**, 693 (1940). Smith, G., and Jones, E. E., *Proc. Soc. Exp. Biol. Med.*, **43**, 157 (1940). *Evans, et al.*, *Proc. Soc. Exp. Biol. Med.*, **46**, 411 (1941).

[415] Rowntree, *et al.*, *Endocrinology*, **23**, 581, 584, 593 (1937).

[416] Hammett, F. S., *Protoplasma*, **7**, 279 (1929); **11**, 383 (1930); *Proc. Am. Phil. Soc.*, **68**, 151 (1929), and many other papers. Voegtlin, C., and Chalkey, H. W., *Public Health Reports*, **45**, 3041 (1931); *Cold Spring Harbor Symposia on Quantitative Biology*, **2**, 84 (1934).

[417] There is a very large literature on this subject which this section does not intend to cover. A few key references: Wendt, F. W., and Thimann, K. V., "Phytohormones", 1937. Boysen-Jensen, P., "Growth Hormones in Plants", 1936. Avery, G. S., Second *Growth* Supplement (1940), p. 73. Wendt, F. W., *American Scientist*, **31**, 189 (1943). Avery, G. S., Jr., also Van Overbeek, J., Hamner, K. C., in *Cold Spring Harbor Symposia on Quantitative Biology*, **10** (1942). Harris, R. S., and Thimann, K. V., "Vitamins and hormones", New York, 1943 and 1944.

[418] Robbins, W. J., *Bot. Gaz.*, **74**, 59 (1922).

[419] White, P. R., *Plant Physiol.*, **9**, 585 (1934).

[420] Robbins and Bartley, M. A., *Science*, **85**, 246 (1937).

[421] Robbins and Schmidt, M. B., *Am. J. Bot.*, **26**, 149 (1939).

[422] Bonner, J., *Science*, **85**, 183 (1937). Bonner and Addicott, F. T., *Id.*, **88**, 577 (1938). Addicott and Devirian, P. S., *Am. J. Bot.*, **26**, 667 (1939).

Auxin is widely distributed, influencing, among other processes, the growth rates and thereby the growth form (Ch. 17) of plant embryos, seedlings, and stems. Many growth peculiarities and abnormalities are supposed to reflect corresponding patterns of auxin distribution. The auxin concentration in given positions may be influenced by temperature, light, gravity, x-rays, ultra-short radio waves, and certain gene peculiarities. Plant curvatures or tropisms (heliotropism, geotropism, etc.) are thus explained by the effect of light, gravity, etc. on the auxin distribution, with resulting differences in growth rates in the different parts. Photoperiodism of plants (Ch. 8) is similarly explained by Hamner. The upright growth of plants against gravity is explained by the pattern of auxin distribution. On the other hand, the "lazy" peculiarity (plant lies on the ground in accordance with gravitational pull) of some corn varieties is explained by lack of ability to shift auxin in response to gravity[425]. Plant dwarfism, as illustrated by the corn variety *nana*, is explained by excessive auxin destruction by the gene *nana*[426], and so on.

The auxin effect on plant growth and development reminds one of the thyroxine effect on animal growth and development and of the influence of temperature and other factors on thyroxine concentration. The *dosage* effect of auxin on plants is similar to that of thyroixine on animals: there is only one optimal dosage; too little or too much leads to unfavorable results[427]. There also appears to be a similarity or analogy between the effects of auxin and thyroxine on "basal metabolism" or respiration rate[428].

7.9: Summary. The introduction (Sect. 7.1) is an extensive summary of this chapter. Emphasis is placed on the interrelations between vitamins (exogenous catalysts) and hormones (endogenous catalysts). Special attention is given to interrelations between the various hormones in reproduction, lactation, growth, and in the metabolism of minerals, carbohydrates, and fat (ketosis); to the danger of disturbing hormonal balance and to the importance of considering incompatibilities between immediate and long-range efficiency of agriculturally productive processes related to hormone administration. The following quotation[429] is an excellent summary of this balance concept.

> "The most important concept in endocrinology which emerges from the feverish activity of the past decade is the principle of endocrine balance. Discovered and rediscovered by several investigators, the paradoxical truth has dawned finally that man or beast may suffer less from the loss of several glands than from losing a single one. For each of the precious juices the other secretions supply a partial antidote, so that health and personality may be preserved, delicately poised. Henceforth the practicing consultant and laboratory investigator, both, must think in terms of integrated hormonal effects".

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[423] Kögl, F., *J. Soc. Chem. Ind.*, **57**, 49 (1938).

[424] For other synthetic plant catalysts, see Zimmerman, P. W., and Hitchcock, A. E., *Contr. Boyce Thompson Inst.*, **12**, 1 (1941); **12**, 321 (1943).

[425] Van Overbeek, J., *Heredity*, **29**, 339 (1938).

[426] Van Overbeek, J., *Plant Physiol.*, **13**, 587 (1938).

[427] Thimann, K. V., *Am. J. Bot.*, **24**, 407 (1937).

[428] Commoner, B., and Thimann, *J. Gen. Physiol.*, **24**, 279 (1941).

[429] Salter, W. T., "The endocrine function of iodine", Harvard University Press, 1940.

Chapter 8

Metabolic Catalysts in the Efficiency Complex: Seasonal Rhythms

> Once in each revolving year
> Gentle Bird! We find thee here;
> When nature wears her summer vest,
> Thou com'st to weave thy simple nest.
> *Anacreon*

> Speaking teleologically, the breeding season is regulated by the times most suitable for the young to be produced and reared. *F. H. A. Marshall*

8.1: Introduction. The sun, some 93 million miles away, is the celestial limiting factor in life processes in furnishing not only energy (Ch. 2) but also catalysts which directly or indirectly condition many activities, one of the most dramatic of which is seasonal sex activity. This is not a new observation, as indicated by the above quotation (cited by Rowan) from Anacreon, 600 B.C. Systematic investigation of the involved clock-like timing is, however, recent. The purpose of this chapter is to present several new observations on the seasonal metabolic and growth rhythms of goats[1] and fowls[2] against the background of the literature.*

An evolutionary understandable but physiologically confusing arrangement is that breeding in different species occurs in different calendar months, depending on the length of the gestation period in relation to food supply and warmth; that is, mating occurs during such time as will be "most suitable for the young to be produced and reared".[3] This means that each species has a different physiologic timing mechanism for responsiveness to the activating agents. Some species are stimulated to sex activity by increasing daylight, or/and increasing temperature (spring), others by decreasing daylight or/and decreasing temperature (late summer, autumn). Maize and soybeans bloom only when the days become shorter and reach a certain limiting *short* day; spinach and wheat bloom only when days become longer and reach a certain limiting *long* day. Deer, sheep, goats, and in general ruminating ungulates tend to come under natural conditions into sex activity when days become shorter; ferret, fox, field mouse, wildcat, hedgehog, and in general carnivors and insectivors, and practically all birds investigated (juncos, crows, canaries, starlings, turkeys, sparrows, doves, ducks, pheasants, quail, grouse) tend to come into sex activity only when days become longer. Horses, having a gestation period of about 11 months, breed in the spring (March-July) so as to foal the following spring.

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[1] Brody, S., Sandburg, Mrs. Carl and Asdell, S. A., Univ. Missouri Agr. Exp. Sta. Res. Bull. 291, 1938. Brody, S., "Temperature factors in animal production," in "Temperature, Its measurement and Control in Science and Industry," Reinhold, 1941.

[2] Winchester, C. F., Univ. Missouri Agr. Exp. Sta. Res. Bull. 315, 1940.

* This chapter overlaps discussions in Ch. 7 on hormones and Ch. 11 on the influence of temperature on life processes (Figs. 11.19 and 11.20, influence of temperature on growth of chickens).

[3] Marshall, F. H. A., *Phil. Trans.*, **226B**, 423 (1936); *Proc. Roy. Soc.*, **122B**, 413 (1937); *Biol. Rev.*, **17**, 68 (1942).

Domestication tends to free animals from the seasonal influence and to shorten the estrus cycles. Thus dogs in the arctic regions have a single sharply-defined breeding period, similar to that of the wolf, jackal, and dingo; the domestic dog in temperate climate breeds twice a year and the time of breeding is not sharply defined. Likewise the wildcat breeds once a year, but the domestic cat breeds several times. The wild rabbit breeds in early spring, the domestic rabbit throughout the year. Wild cattle, like deer, breed in the autumn so as to calve in the spring; domestic cattle breed throughout the year. Domestic sheep, goats[4], horses, and other species, however, still tend to cling to a more or less seasonal rhythm[5].

Species evolved in the tropics and subtropics do not respond sexually to seasonal light stimuli. Thus the sex activity of guinea pig, guinea fowl[6], subtropic deer[7], and primates[8] are apparently independent of season. The problem was recently debated[9] as to whether primitive man, and contemporary man in the arctic, is seasonal, but with no conclusive decision. Fitt published an impressive essay on the seasonal rhythm in man, on the effect of spring.

"A spring rousing which is not merely a mechanical, physical process, but a highly emotional one as well, associated with the demands of the reproductive instinct, characterized by haste, restlessness, and a high measure of instability. This phase continues through the spring and summer until later, with autumn or thereabouts, the consolidating, quieter phase sets in. This rhythm shows man to be still a creature of the sun, dependent upon its course through the seasons"[10].

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[4] Bissonnette, T. H., "Breeding cycle in goats," *Physiol. Zool.*, **14,** 379 (1941).

[5] Cf. Asdell, S. A., *J. Agr. Sci.*, **16,** 632 (1926) (goats). Turner, C. W., *J. Dairy Sci.*, **19,** 619 (1936) (goats). Kupper, M., Union South Africa Dept. Agr., 13th and 14th reports. Director Vet. Ed. and Res. Part II, p. 1211, 1928 (cattle, sheep, goats, donkeys, horses). Villegas, V., *Phillip. Agr.*, **17,** 477 (1918) (horses, cattle, water buffalo, sheep, goats).

[6] Scott, H. M., and Payne, L. F., *Poultry Sci.*, **16,** 90 (1937).

[7] Marshall,[3] 1942.

[8] Zuckerman, S., "The social life of monkeys and apes," London, 1937.

[9] Llewelyn, L. T., "Seasonal rhythm in Eskimos," *Nature*, **129,** 868 (1932). Huntington, E., "Season of birth: its relation to human abilities," Wiley, 1938. Whitaker, W. L., *Science*, **88,** 214 (1938); Ashley-Montague, M. F., *Id.*, **89,** 290 (1939). Darby, Hugh, and Childs, D., Am. Assn. Adv. Sci. Meeting, Jan. 1941 (Spring increase in estrogens). See also books on climate by Drs. C. A. Mills and W. F. Petersen.

In brief, under natural conditions and in regions which have sharply defined climatic seasons, plants and animals pass a seasonal reproductive—and productive—rhythm, so adjusted as to be most favorable for the rearing of the young. The physiologic mechanisms whereby the sex activities are set into motion at different calendar months remain to be worked out and applied for increasing the efficiency (more frequent reproduction) and profit (as, for example, by "hatching pheasant chicks on Christmas day"[11]) of productive processes.

8.2: Historical notes. In 1913 Turnois[12] observed that sex activity in some plants depends on days of definite duration. About 1920 Garner and Allard[13] began publishing data on sex activity in plants in relation to daylight duration. They called this phenomenon *photoperiodism*. Since then a large literature has developed on the timing and on the mechanisms involved[14].

Photoperiodicity in animals was discovered in connection with investigations of the mechanism of seasonal bird migration. In 1907 Sharpey-Schafer[15] expressed the opinion that the ratio of daylight to darkness determines the seasonal migrations of birds "in consequence of the necessity to most birds of daylight for procuring food". It was known that the (spring) northward migration of birds is associated with enormous gonadal development. But this was attributed to temperature. Rowan[16] first (1925) approached this problem experimentally, disproved the temperature theory for birds, and demonstrated that migration is dependent on light and "hormone elaborated by the developing gonads" (1938). Rowan substantiated the photoperiodic theory by subjecting juncos (finch) and crows to increasing daylight in December. "By the end of December, in spite of minimum reading of 52° below zero F, the birds that had been kept on increasing day length were singing and their gonads maturing". Electric lights (devoid of ultra-violet) were used in these experiments. The birds were brought into breeding condition or quiescence simply by lengthening or shortening the period of light exposure. However, the birds did not breed, because of inhibitory effects of captivity on the breeding habits of juncos. There is a difference between breeding condition and actual breeding[17].

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[10] Fitt, A. B., *Rep. 16th Meet. Australasian Assn. Adv. Sci.*, **16**, 704 (1924).

[11] Bissonnette, T. H., and Czech, A. G., *Am. Naturalist*, **71**, 525 (1937).

[12] Turnois, J., *Compt. rend. Acad. Sci.*, **155**, 297 (1912).

[13] Garner, W. W., and Allard, H. A., *J. Agr. Res.*, **18**, 553 (1920). Allard, H. A., *Id.*, (Nov. 15, 1938). Hamner, K. C., *Bot. Gazz.*, **99**, 615 (1938). Loewhwright, W. F., *Bot. Rev.* (Nov., 1938). Murrneck, A. E., Univ. Missouri Agr. Exp. Sta. Res. Bull. 268, 1937.

[14] See, for example, Hamner, K. C., and Bonner, J., *Bot. Gazz.*, **100**, 388 (1938). Bennett, J. P., and Shook, F., *Plant Physiology*, **13**, 219 (1938).

[15] Schafer, E. A., *Nature*, **77**, 159 (1907).

[16] Rowan, W., *Nature*, **115**, 494 (1925). For a full review of his work, see Rowan, *Biol. Rev.*, **13**, 374 (1938).

[17] Rowan, W., *Proc. Nat. Acad.*, **18**, 639 (1932).

Bissonnette[18] confirmed Rowan's results on starlings. Bissonnette[19] and Baker and Ranson[20] extended the results to mammals.

While the seasonal reproductive periodicity in animals investigated by Rowan and by Bissonnette is photoperiodic (stimulus from visible radiations), there are many examples of thermoperiodic sex responses (stimulus from infrared radiations). Thus the breeding cycle in the white rat may be lengthened by lowering the room temperature[21]. Ovulation in bats will occur any time after the middle of February (in Columbia, Mo.) if they are brought into a warm room[22]; but this varies with dietary and other habits of the particular bat[23].

Marshall reported that temperature is an important contributing factor to reproductive activities in deer:

"There is a common belief which is well attested that in deer general rut does not occur properly until there has been a sharp frost, that is to say, that a frost will awake both stags and hinds to their full sexual activity . . . if there is an exceptionally mild autumn, such as occurs only once or twice in a half-century, there is very little mating, and very few calves will be dropped in the following spring"[24].

The annual sex periodicity of the 13-lined ground squirrel is apparently not at all influenced by light.[25] The sex rhythm in the male[26] appears to be the same in "field" animals in dark hibernating burrows under natural conditions of life and in animals exposed to light rhythms in the laboratory. Moreover, ground squirrels, like deer, require a cool spell (+4°C) to enable them to breed[27]. The pituitaries of these animals showed a seasonal rhythm in gonadotropic activity regardless of light effects.

It is generally known that plants respond to periodic thermal treatment. Such thermoperiodic induction is known by various names, such as "vernalization". When winter wheat is exposed during germination to a temperature a little above freezing, it will flower and fruit the same year, though sown in the spring. It is generally known that certain plants have to be nearly frozen every winter to make them grow the following spring.

8.3: Mechanisms of seasonal sex periodicity. It is agreed that sex activity has its basis in endocrine mechanisms controlled by the anterior pituitary. But sex activity is also dependent on many other factors such, for example, as food. Light happened to be the *limiting* factor in the junco, crow, starling, ferret, and so on. Rowan[28] suggested that increased exercise associated with longer days might possibly be the "cause" of greater sex activity. However, Bissonnette[29] did not find this for the starling, and observed that ferrets responded to light even if they could not move, even when they were approaching death from tuberculosis.

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[18] Bissonnette, T. H., *Am. J. Anat.*, **45**, 289 (1930); *J. Exp. Zool.*, **58**, 281 (1931).

[19] Bissonnette, T. H., "Reaction of ferrets to light", *Proc. Roy. Soc.*, **110B**, 322 (1932).

[20] Baker, J. R., and Ranson, R. M., "Breeding in field mice," *Id.*, p. 313.

[21] Cf. Lee, M. O., *Am. J. Physiol.*, **78**, 246 (1926).

[22] Guthrie, M. J., "Reproductive cycles in animals with special reference to the bat", *Growth*, **3**, 261 (1939).

[23] Baker, J. R., *J. Linn. Soc.* (*Zoology*), **40**, 123, 143 (1936).

[24] Marshall, F. H. A.[3], 1937.

[25] *Cf.* Moore, C. R., Simmons, G. F., Wells, L. J., Zalesky, M., and Nelson, W. O., *Anat. Rec.*, **60**, 279 (1934).

[26] Wells, L. J., *Id.*, 409 (1935).

[27] Zalesky and Wells, *Physiol. Zool.*, **13**, 268 (1940).

It has been established that the pituitary in photoperiodic animals responds with profound histological changes to changes in the day/night ratio[30], and that hypophysectomized ferrets are unaffected by light variations.[31] However, the later observation is, perhaps, without significance because hypophysectomy abolishes sex activity and subjecting to light does not regenerate the pituitary.

Assuming that light exerts its seasonal effect by way of the pituitary, several investigated the path of transmission of the stimulus. Reports indicate that cataract of both eyes[32] (but not of one[33]) abolishes estrus for some time, as does cutting the optic nerve (in ferrets)[34], and there develops instead an inherent sex cycle by "alternate rise and fall in secretion or liberation of gonadotropic hormones"[35], independently of light.

In brief, blind photoperiodic animals tend to have their photoperiodic cycle replaced by an "inherent" sex cycle independent of the light periodicity. This inherent cycle is apparently not as reliable as the photoperiodic cycle[36]. Covering the eyes also tends to disturb the photoperiodic sex effect[37]. However, this is not always the case[38].

Summarizing, the eye is normally the light receptor in photoperiodic animals. When the eye is removed, the optic nerve may, perhaps, serve as receptor when light is directed into the eye socket (Benoit); the naked skin may, perhaps, be a receptor (Ivanova). The light probably initiates nervous impulses which travel to the hypophysis by way of the hypothalamus[39]. Some species are freed from the photoperiodic influence by domestication, that is, by supplying food and warmth throughout the year, indicating that photoperiodicity is dependent on many other factors, food and warmth being the most obvious.

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[28] Rowan, W., *Nature*, **115**, 494 (1925); **122**, 11 (1928).

[29] Bissonnette, T. H., *Science*, **76**, 253 (1937); *Biol. Bull.*, **65**, 452 (1933); *Quart. Rev. Biol.*, **8**, 201 (1933).

[30] Bissonnette, T. H., *Biol. Bull.*, **68**, (1935); *J. Exp. Zool.* (Aug., 1935); *Anat. Rec.* (Sept., 1935).

[31] Hill, M., and Parkes, A. S., *Proc. Roy. Soc.*, **115B**, 14 (1933). Bissonnette, T. H., *Endocrinology*, **22**, 92 (1938); *J. Comp. Psychol.*, **22**, 93 (1936).

[32] Marshall, F. H. A., and Bowden, F. P., *J. Exp. Biol.*, **11**, 409 (1934); **13**, 383 (1936).

[33] Bissonnette, T. H., *Proc. Roy. Soc.*, **110B**, 322 (1932); *Quart. Rev. Biol.*, **8**, 210 (1933); **11**, 371 (1936).

[34] Bissonnette, T. H., *J. Heredity*, **27**, 171 (1936).

[35] Bissonnette, T. H., *Endocrinology*, **22**, 92 (1938).

[36] Clark, W. E., *et al.*, *Proc. Roy. Soc.*, **126B**, 449 (1939).

[37] Benoit, J., *Compt. rend. Acad. Sci.*, **199**, 167 (1934). Ringoen, A. R., and Kirchbaum, A., *J. Exp. Zool.*, **80**, 173 (1939).

[38] Benoit, *Compt. rend. Acad. Sci.*, **201**, 359 (1935), and many papers thereafter. Riley, G. M., and Witschi, E., *Anat. Rec.*, **70**, 50 (1937) (Suppl.). Whitaker, W. L., *J. Exp. Zool.*, **83**, 33 (1940).

[39] Guthrie, M. J., *Growth*, **3**, 267 (1939). Haterius, H. O., *Cold Spring Harbor Symposium on Quantitative Biology*, **5**, 280 (1937). Clark, W. E., *et al.*,[36] 1939.

8.4: Seasonal food supply rhythms in relation to seasonal sex activity. There is a seasonal rhythm not only in the amount but also in the nature of the food supply, herbage, and other feeds and foods. Milk is much richer in vitamin D (Fig. 8.1A)[40], vitamin A (Fig. 8.1B)[41], and in other vitamins and fatty acids[42] in summer than in winter. (Compare the seasonal rhythm in vitamin D concentration, Fig. 8.1A, with that of the ultraviolet radiation, Fig. 8.5C.) There are similar seasonal rhythms in vitamin D, phosphorus, and calcium concentration in blood, which are opposite in trend to the seasonal incidence in rickets[43]. A reproductive aspect of vitamin D or sunlight is illus-

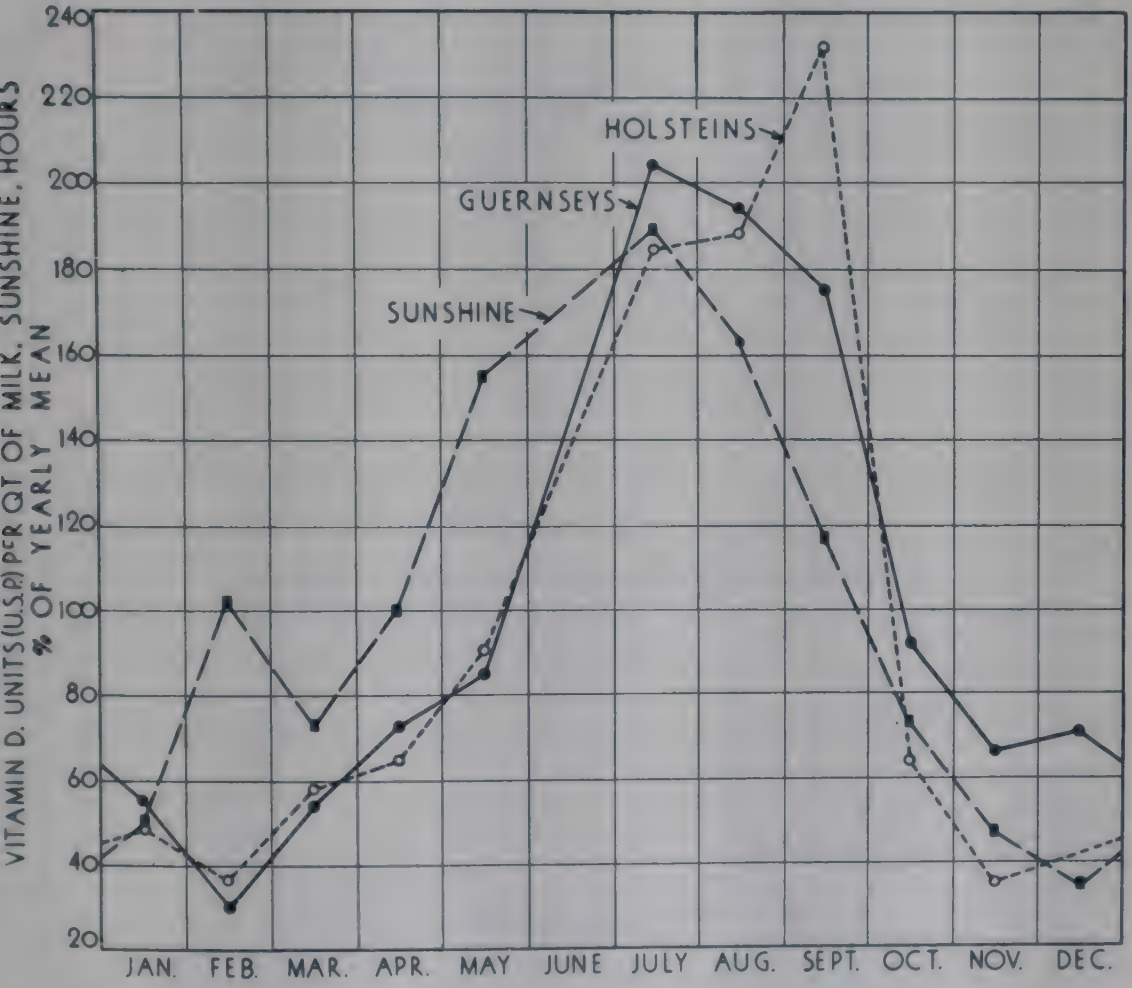

Fig. 8.1a—Seasonal rhythm of vitamin D concentration in milk.

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[40] Recomputed from Bechtel, H. E., and Hopper, C. A., *J. Nut.*, **11,** 537 (1936).

[41] Recomputed from Dornbush, A. C., Peterson, W. H., Olson, F. R., *J.A.M.A.*, **114,** 1748 (1940).

[42] Booth, R. G., Kon, S. K., Dann, W. J., and Moore, T., *Chem. Ind.*, **52,** 270 (1933). *Biochem. J.*, **27,** 1189 (1933); **29,** 133 (1935).

[43] See, for example, Hess, A. F., and Lundhagen, M. A., "A seasonal tide of blood phosphate," *J. Am. Med. Assn.*, **79,** 2210 (1922). Tisdall, F. F., and Brown, D., "Seasonal variation of the antirachitic effect of sunshine," *Am. J. Dis. Child.*, **34,** 721 (1927). Brun, K., "Seasonal variations in the phosphate content of the blood," *Acta Pediatrica*, **7,** Supp. 2, p. 226 (1928). Baldwin, H. and R., *Am. J. Dis. Child.*, **34,** 994 (1927).

trated by the result of Lucas, Hume and Smith[44], whose marmosets refused to take cod liver oil and failed to breed. Irradiation with ultraviolet light corrected the breeding difficulty.

Friedman[45] reported the presence of gonad-stimulating substances in immature oat plants, sudan grass, corn plants (but not in kidney beans, brown corn, sorghum, or soybeans). Injecting 60 mg of one plant preparation produced ovulation in the rabbit and ovarian stimulation in the rat. Copper salts, in which immature plants are rich, are also gonadotropic[45], or at least augment the activity of the gonadotropic hormones; 3.5 mg copper (as sulfate or acetate) produced ovulation in the rabbit. Young grasses are rich in many other factors such as the "grass-juice" factor, vitamin E, vitamin A, vitamin B complex (Ch. 6), and limiting amino acids[46].

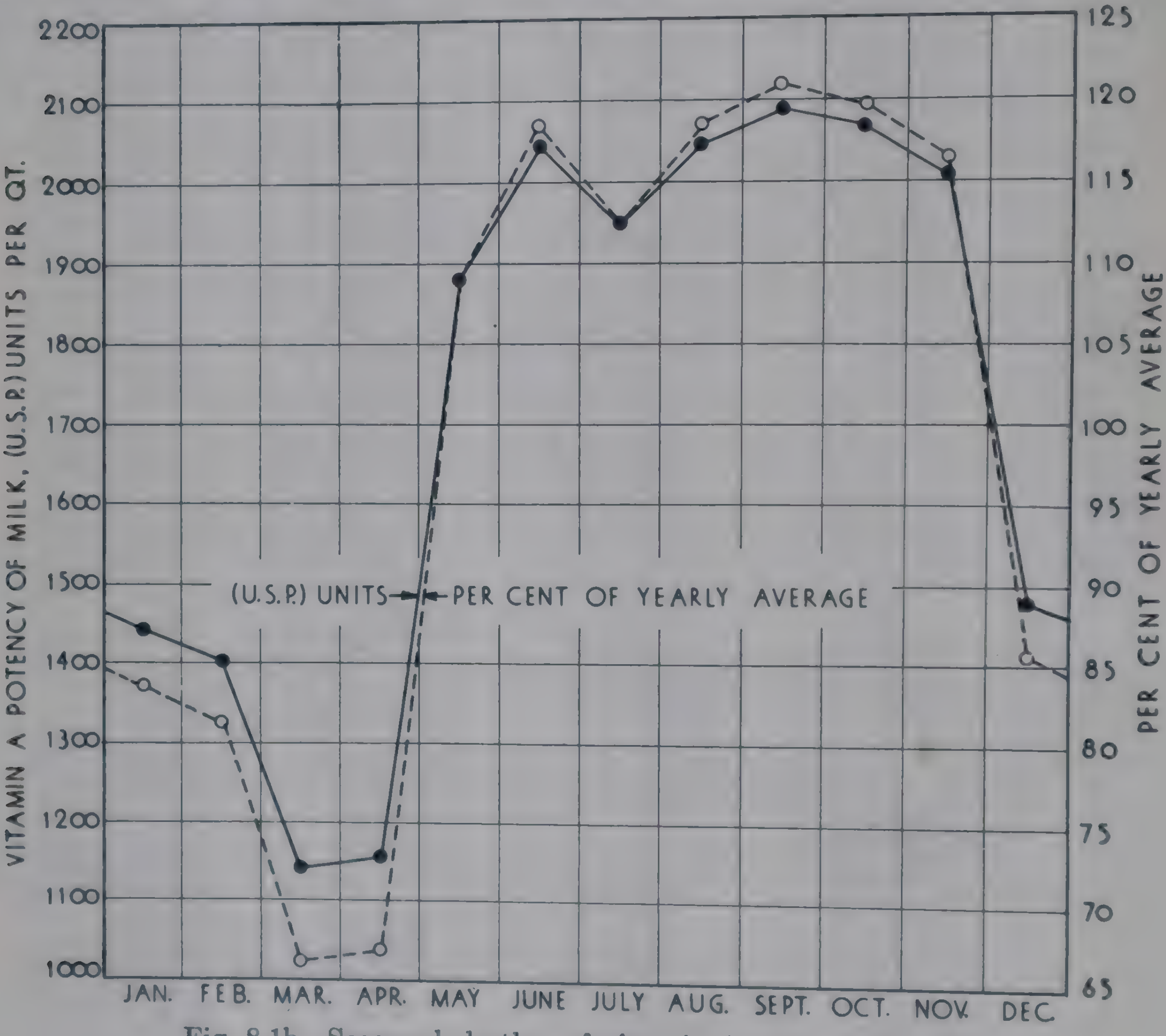

Fig. 8.1b—Seasonal rhythm of vitamin A potency in milk.

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[44] Lucas, J. H., Hume, E. M. M., and Smith, H. H., *Proc. Zool. Soc.*, **1927**, 447.

[45] Friedman, M. H., and G. S., *Am. J. Physiol.*, **125**, 486 (1939); **128**, 492 (1940). Breneman, W. R., "Augmentation of pituitary gonadotropic hormone by chlorophyll, plant growth hormones and hemin," *Endocrinology*, **74**, 488 (1939). Emmens, C. W., "Ovulation following injection of copper salts," *J. Endoc.*, **2**, 63 (1940). Fevold, H. L., Hisaw, F. L., and Greep, R., *Am. J. Physiol.*, **117**, 68 (1936).

[46] Pearson, P. B., Hart, E. B., and Bohstedt, G., "Quality of protein and the estrous cycle," *J. Nut.*, **14**, 329 (1937). Guilbert, H. R., and Goss, E., *Id.*, **5**, 251 (1932).

The seasonal thyroid rhythm (Figs. 8.2A[47] and 8.2B[48]) may be related to the seasonal rhythms in availability of iodine and related dietary constituents. As might be expected from the seasonal food-supply rhythms, the iodine percentage in the thyroid increases in spring, reaching a maximum in summer (July) and declining thereafter to a minimum in late winter. The size of the gland tends to follow an opposite course. There is no rhythm in iodine content of blood[49]. The thyroid is an important factor in the reproductive and productive processes (Ch. 7).

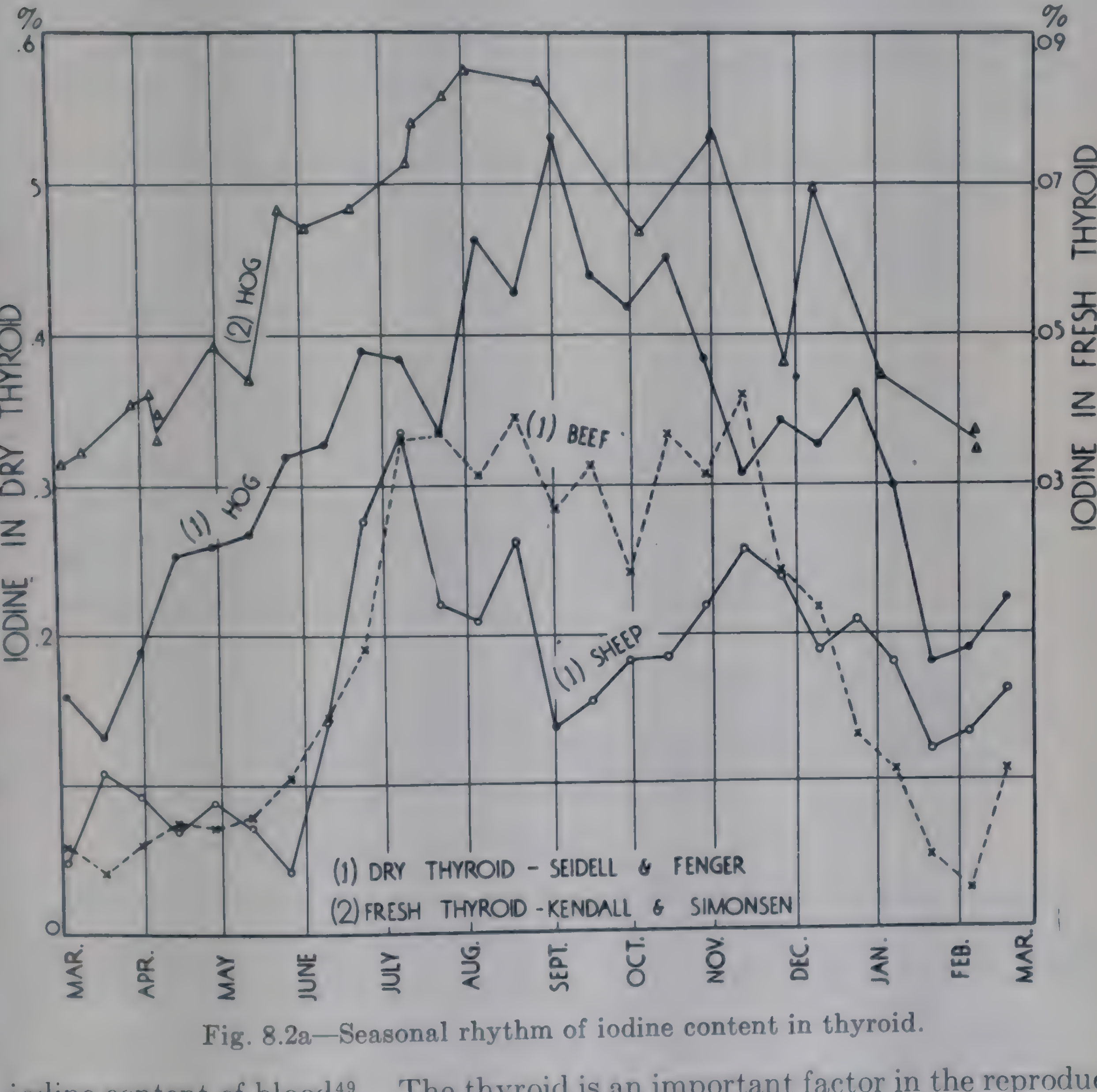

Fig. 8.2a—Seasonal rhythm of iodine content in thyroid.

8.5: Seasonal periodicity in relation to efficiency with special reference to egg and milk production. Reproductive efficiency, of course, increases with increasing reproductive frequency (see Figs. 8.3 and 8.4), and the profit increases on timing the breeding to suit the convenience of the farmer. The following examples indicate the potentialities of this type of research.

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[47] Seidell, A., and Fenger, F., *J. Biol. Chem.*, **13,** 517 (1913). Kendall, E. C., and Simonsen, D. G., *Quart. J. Exp. Biol. Med.*, **6,** 65 (1929).

[48] Cruickshank, E. M., "Factors affecting size and iodine content of the fowl thyroid," Proc. 4th World's Poultry Congress, p. 237, 1930, and *Biochem. J.*, **23,** 1044 (1929). Riddle, O., *Endocrinology*, **11,** (1927); "Seasonal variation in thyroids and adrenals," *Am. J. Physiol.*, **73,** 5 (1925). Riddle and Fisher, *Id.*, **72,** 464 (1925).

[49] Salter, W. T., "Fluctuations in body iodine," *Physiol. Rev.*, **20,** 345 (1940). Clark, E. L., and Boyd, E. M., *J. Biol. Chem.*, **135,** 691 (1940).

Ferrets were brought into estrum during the winter season by the use of light[50]. Similar results were obtained on field mice[51]. Winter breeding was induced[52] in the raccoon, pheasant, quail, and ferret. Cole[53] obtained eggs from mourning doves months earlier than the usual laying season by appropriate light conditions. Grouse[54] were brought into laying about 1 month earlier by continuous lighting (not changing day-to-night ratios) beginning February 10.

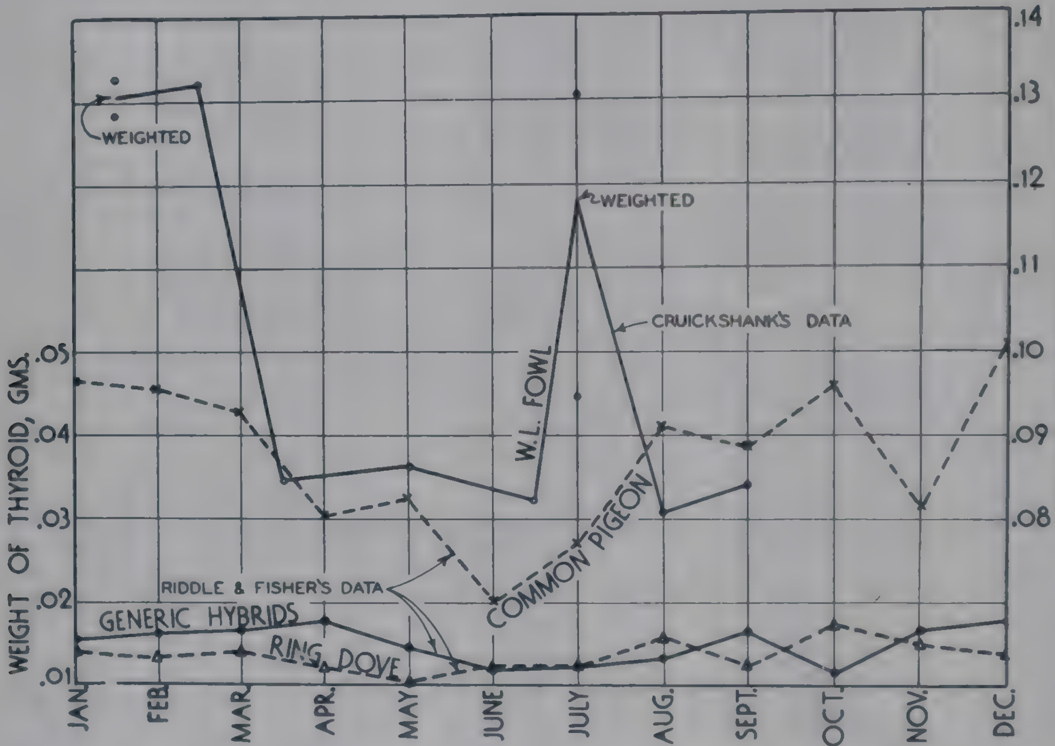

Fig. 8.2b—Seasonal rhythm in thyroid weight.

Poikilotherms are also photoperiodic; Hoover[55] induced winter breeding in brook trout 3 to 3½ months earlier than the normal spawning season. Scott and Payne[56] found that May-hatched turkeys exposed to electric lights from

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[50] Bissonnette, T. H., *Proc. Roy. Soc.*, **110B**, 322 (1932). Hill, M., and Parkes, A. S., *Id.*, **115B**, 14 (1934).

[51] Baker, J. R., and Ranson, R. M., *Id.*, **110B**, 313 (1932); **112**, 39 (1932); **113**, 486 (1933).

[52] Bissonnette and Czech, A. G., "Fertile matings of raccoons in December instead of February induced by increasing daily periods of light," *Proc. Roy. Soc.*, **122B**, 246 (1937); "Eggs by pheasants and quail induced by lighting," *Science*, **83**, 392 (1936). "Hatching pheasant chicks on Christmas day," *Am. Naturalist*, **71**, 525 (1937). Bissonnette and Bailey, E. H., "Litters from ferrets in January induced by increased exposures to light after nightfall," *Am. Naturalist*, **70**, 454 (1936). Burger, J. W., "Experimental photoperiodicity in the male turtle," *Am. Naturalist*, **71**, 481 (1937).

[53] Cole, L. J., *Auk*, **50**, 284 (1933).

[54] Clark, L. B., Leonard, S. L., and Bump, G., *Science*, **85**, 339 (1937).

[55] Hoover, E. E., *Science*, **86**, 425 (1937).

[56] Scott, H. M., and Payne, L. F., *Poultry Sci.*, **16**, 90 (1937); for use of colored lights in the study of egg clutching, see Warren, D. C., and Scott, H. M., *J. Exp. Zool.*, **74**, 137 (1936).

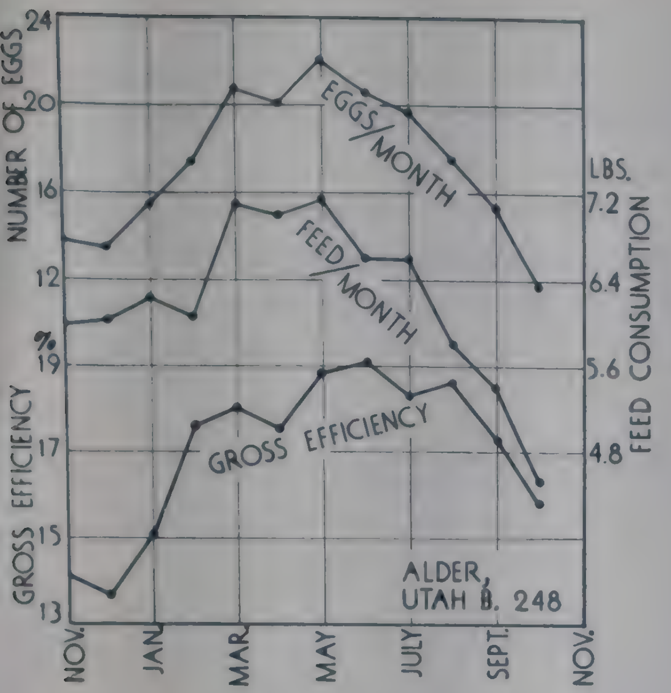

Fig. 8.3—Parallelism between the seasonal rhythms of productivity and gross efficiency of egg production.

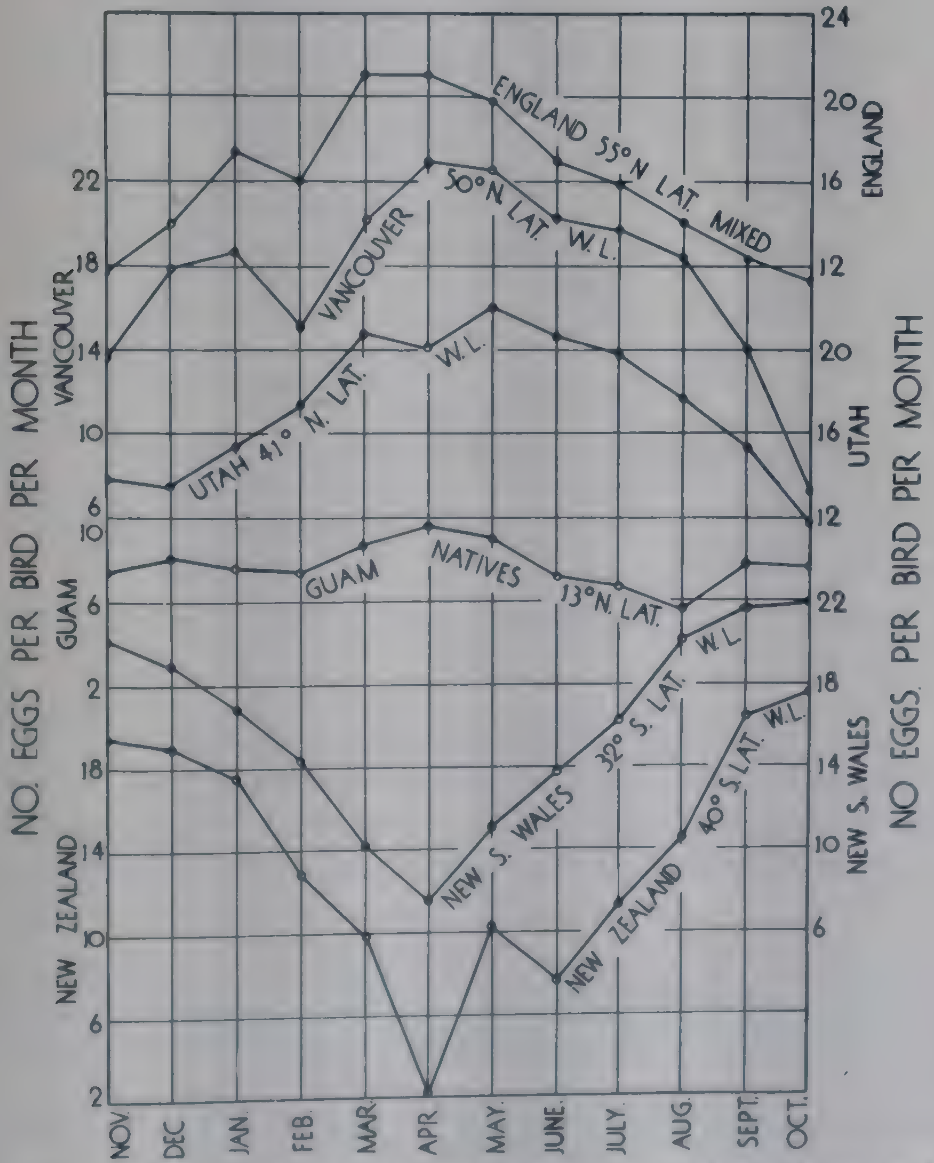

Fig. 8.4—The influence of latitude on the seasonal rhythms of egg production.

4:30 a.m. until natural daylight, during December, were brought into egg production in January, whereas control birds produced no eggs until early March. Only white light or longer wave-lengths stimulated early production; blue light failed to exert this effect.

There are many reports[57] on the use of light in poultry houses for increasing egg production in winter. But such winter lighting is not photoperiodic in the sense of gradual increase or decrease of light. The lights are turned on at 4 or 5 a.m., merely giving the birds a "longer working day" during the period when egg prices are high. The following statistical data on the seasonal rhythm in egg production are cogent in this connection[58].

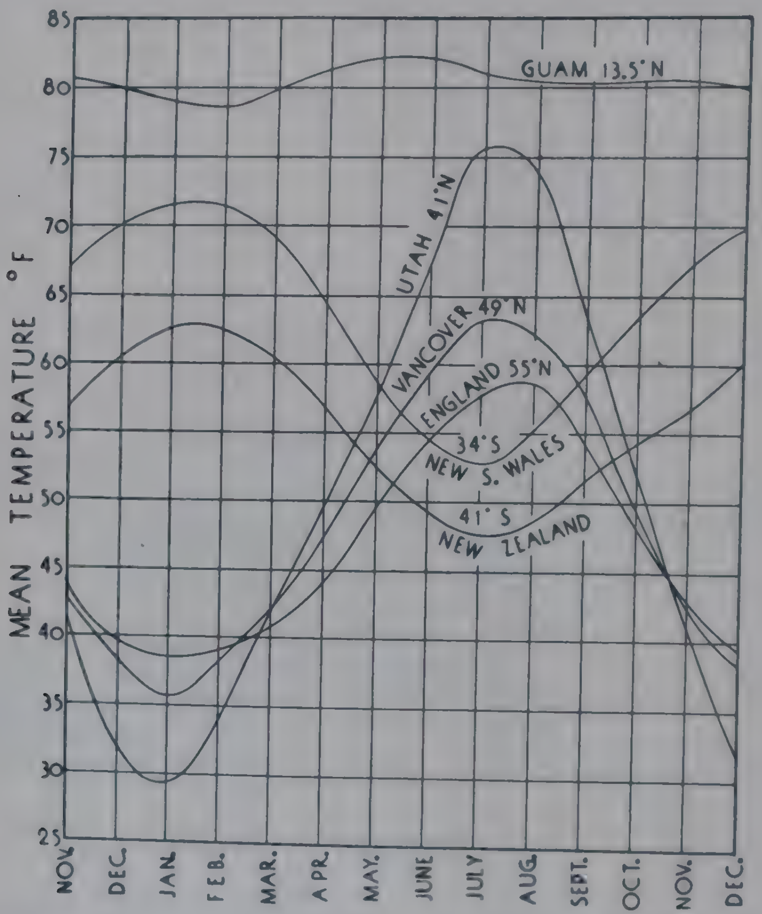

Fig. 8.5a—Monthly temperature rhythms corresponding to the latitudes given in Fig. 8.4.

Fig. 8.4 shows that near the equator, egg production in the domestic fowl is relatively uniform throughout the year; in the upper latitudes of northern hemisphere, maximum production is in April and minimum is October-November; in the southern hemisphere, maximum production is in October-November and minimum in April.

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[57] *Cf. inter alia*, Kable, G. W., Fox, F. G., and Lunn, A. G., "Electric lights for increasing egg production," Ontario Ag. Coll. Sta. Bull. 231, 1928. Parkhurst, R. T., "Artificial illumination to increase winter egg production," J. Min. Agr. Great Britain, 1930, p. 960; Bausman, R. O., "Artificial light and egg production," Directors' Report, Delaware Agr. Exp. Sta. Bull. 205, 1936, p. 10, and many others.

[58] *Cf.* Whetham, Elizabeth, "Factors modifying egg production with special reference to seasonal changes," *J. Agr. Sci.*, **23,** 383 (1933).

Corresponding to the dependence of egg production on latitude, Marshall's[59] observation on the sex behavior of sheep and deer may be cited. After being transported from the northern to the southern hemisphere, sheep and deer bred not in the customary calendar month but in the month corresponding to autumn in the new latitude.

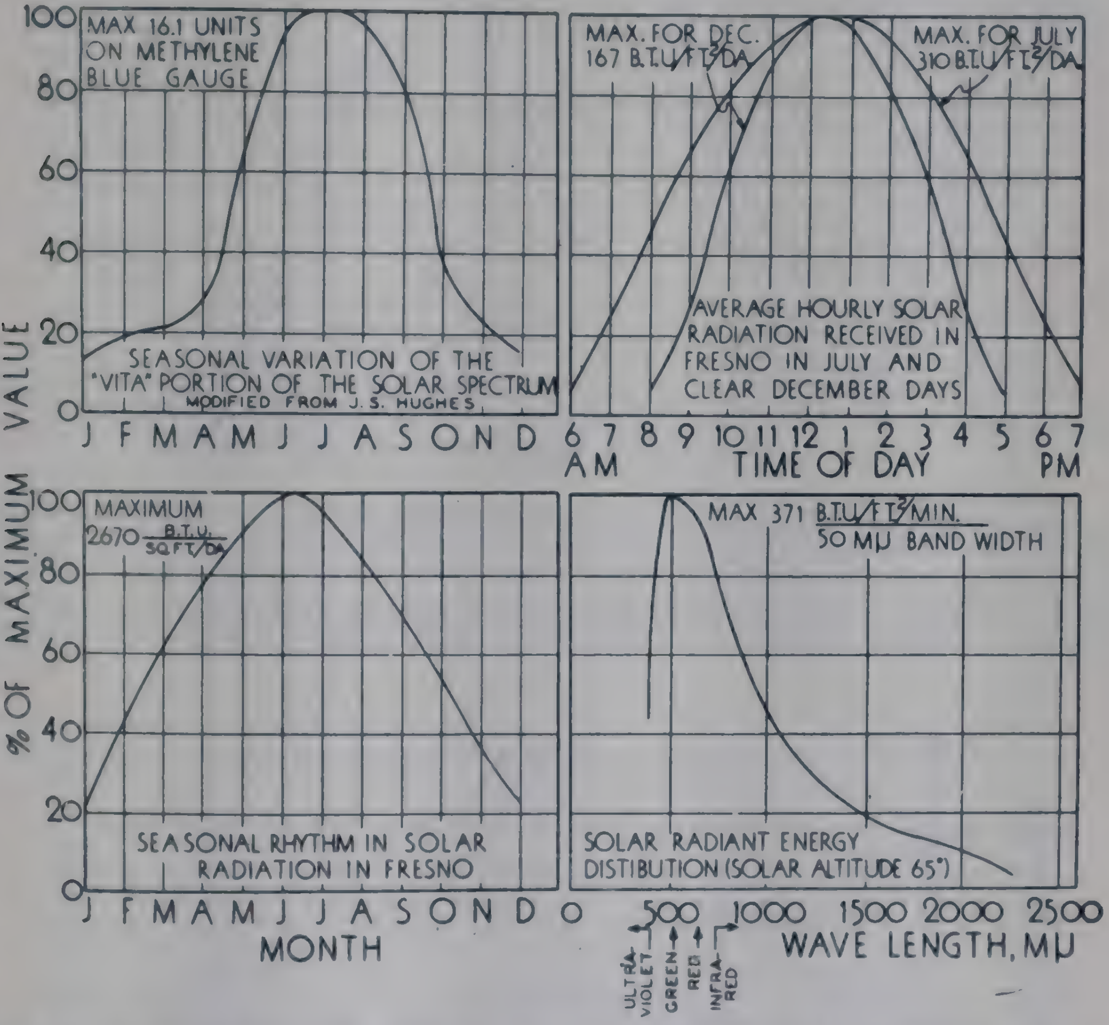

Fig. 8.5b—Monthly sunlight rhythm, average and possible in Cleveland, Ohio, data by Luckiesh et al. Courtesy J. P. Ditchman, General Electric Co.

The corresponding curves for average sunshine and temperature are shown in Fig. 8.5, which indicates the nature of the parallelism between the course of seasonal sex activity in the fowl and the course of seasonal changes in daylight duration.

Dr. V. S. Asmundson[60], University of California, has kindly furnished data on the seasonal rhythm of egg production in the turkey, which we plotted in Fig. 8.6. The broken curves in Fig. 8.6 indicate the seasonal sunshine rhythms

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[59] Marshall, F. H. A., 1936³.

[60] Asmundson, V. S., and Lloyd, W. E., "Effect of season on growth and feed consumption of turkeys," *Poultry Sci.*, **15**, 186 (1936).

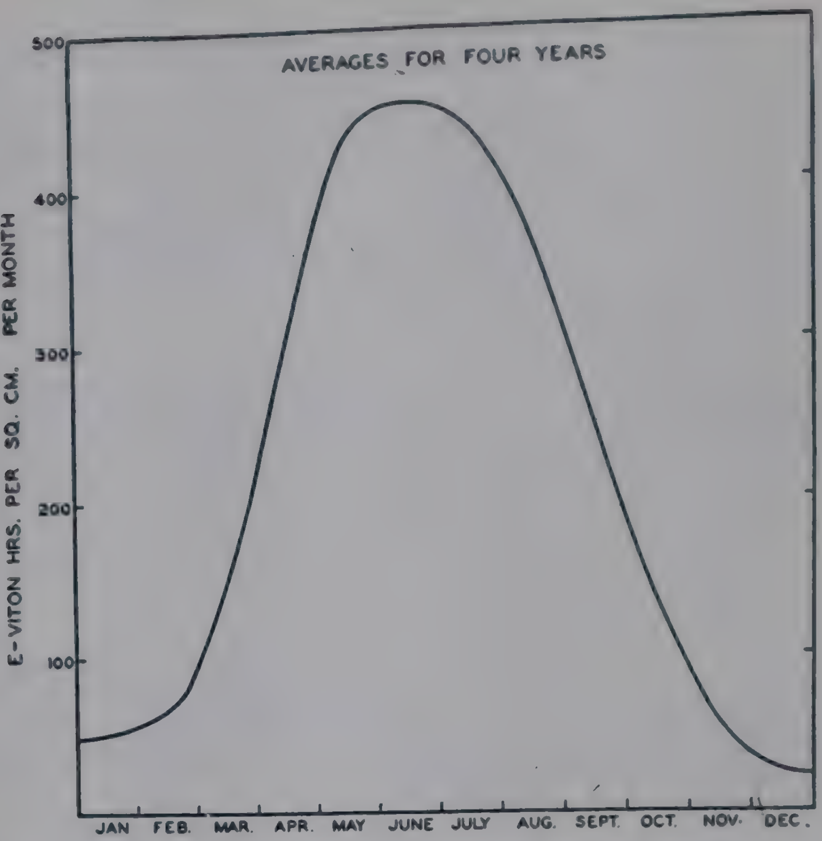

Fig. 8.5c—Monthly rhythm of erythemal ultraviolet energy in daylight, average for four years, in Cleveland, Ohio. (The unit of ultraviolet energy is the "E-viton", equivalent to 10 microwatts of ultraviolet energy after being weighted according to the erythemal response to equal amounts of energy of various wave lengths.) Courtesy J. P. Ditchman, General Electric Co. (data by Luckiesh, Taylor, and Kerr—Cleveland, Ohio).

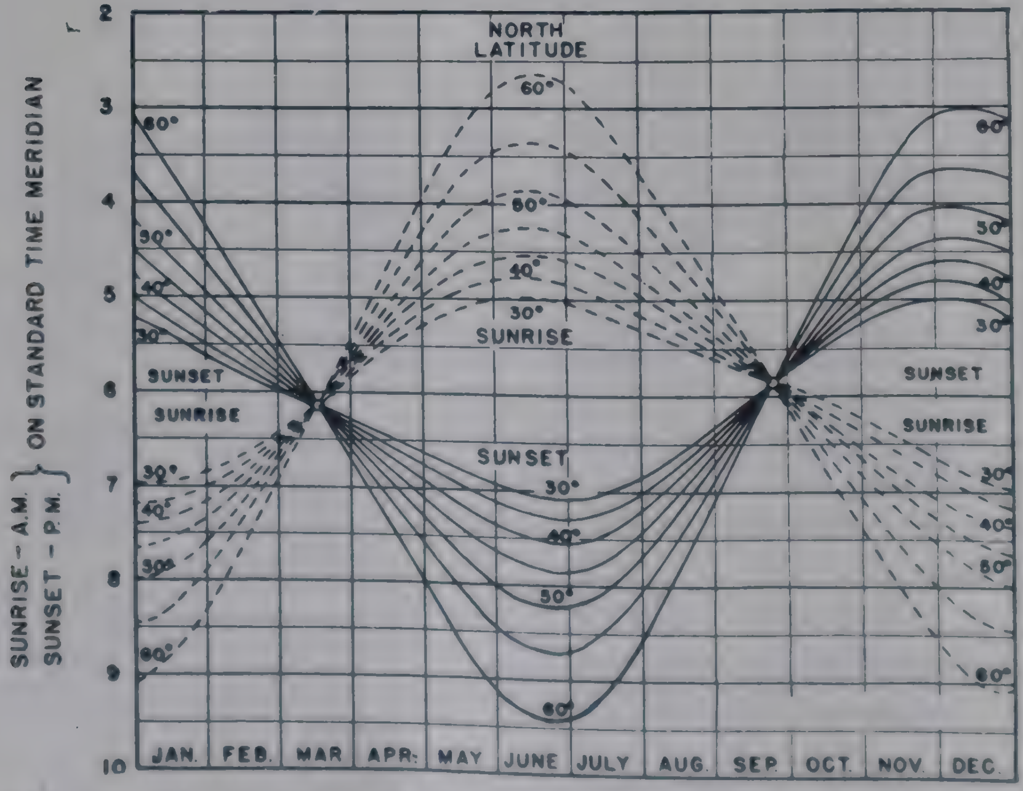

Fig. 8.5d—Monthly rhythm of standard time of sunrise and sunset, north latitudes 30° to 60°. Courtesy J. P. Ditchman, General Electric Co.

as published by the San Francisco Weather Bureau. Fig. 8.6 is also interesting in that it shows the decline in egg production with increasing age. A similar chart for the fowl is shown in Fig. 8.8. Professor E. M. Funk of the University of Missouri kindly supplied data on egg production in quail, plotted in Fig. 8.7.

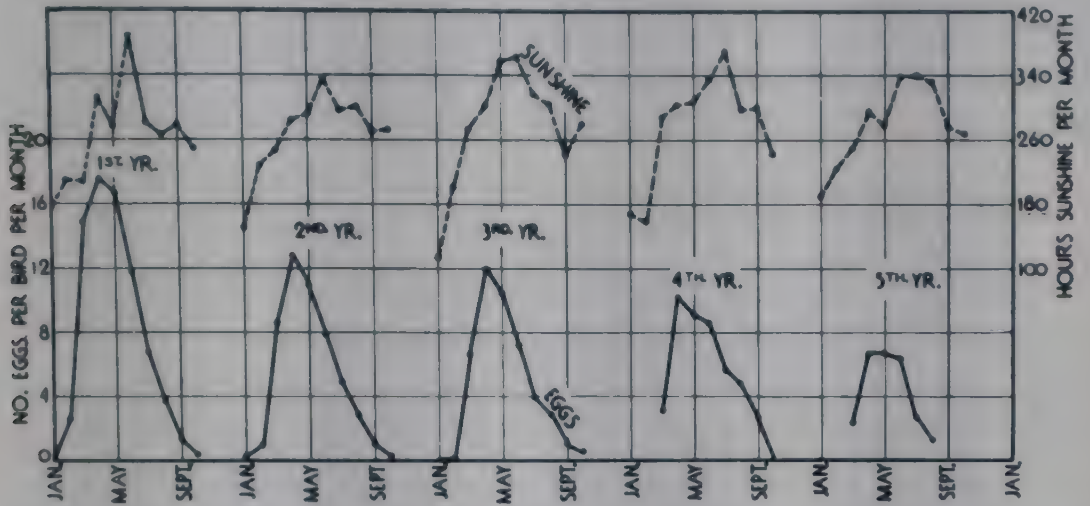

Fig. 8.6—Seasonal rhythm in egg production of turkeys plotted by us from unpublished data by Dr. V. S. Asmundson, University of California. The sunshine curves are from the San Francisco Weather Bureau.

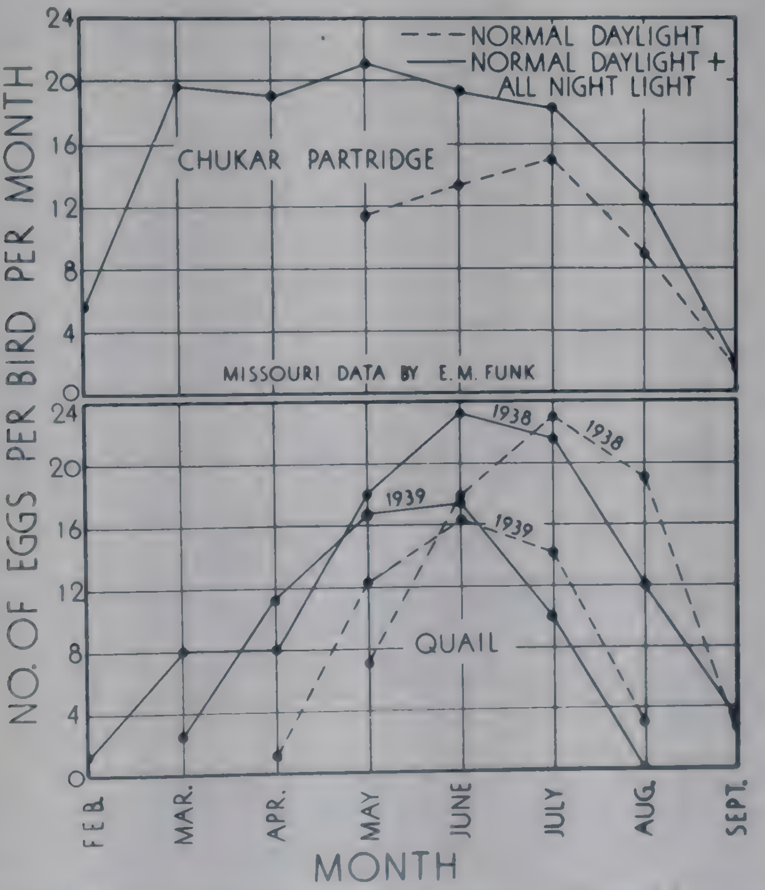

Fig. 8.7—Seasonal rhythm of egg production in quail. Plotted from unpublished data by E. M. Funk of this Station.

We are not familiar with experimental investigations on photoperiodic responses of domestic mammals, although goats[61] and sheep offer suitable material for such work.

Just as egg production in birds is maximal in spring, so is milk production in mammals (Fig. 8.9). It so happens that spring is not only the season of birth under primitive or natural conditions, but is also the season in which pasture is in its prime as nutrient for milk production, and the temperature is most favorable. The high spring milk production is probably the resultant of all these factors, but mostly of feed and temperature. As summer advances, the temperature rises (cattle are exceedingly sensitive to high temperatures Ch. 11, Fig. 11.17), feed quality declines, insects become more pestiferous and perhaps the primitive or "natural" lactation urge tends to terminate. All these factors probably contribute to the late summer decline in milk production, but temperature and decline in the nutritional quality of the feed, are most important (Fig. 810b).

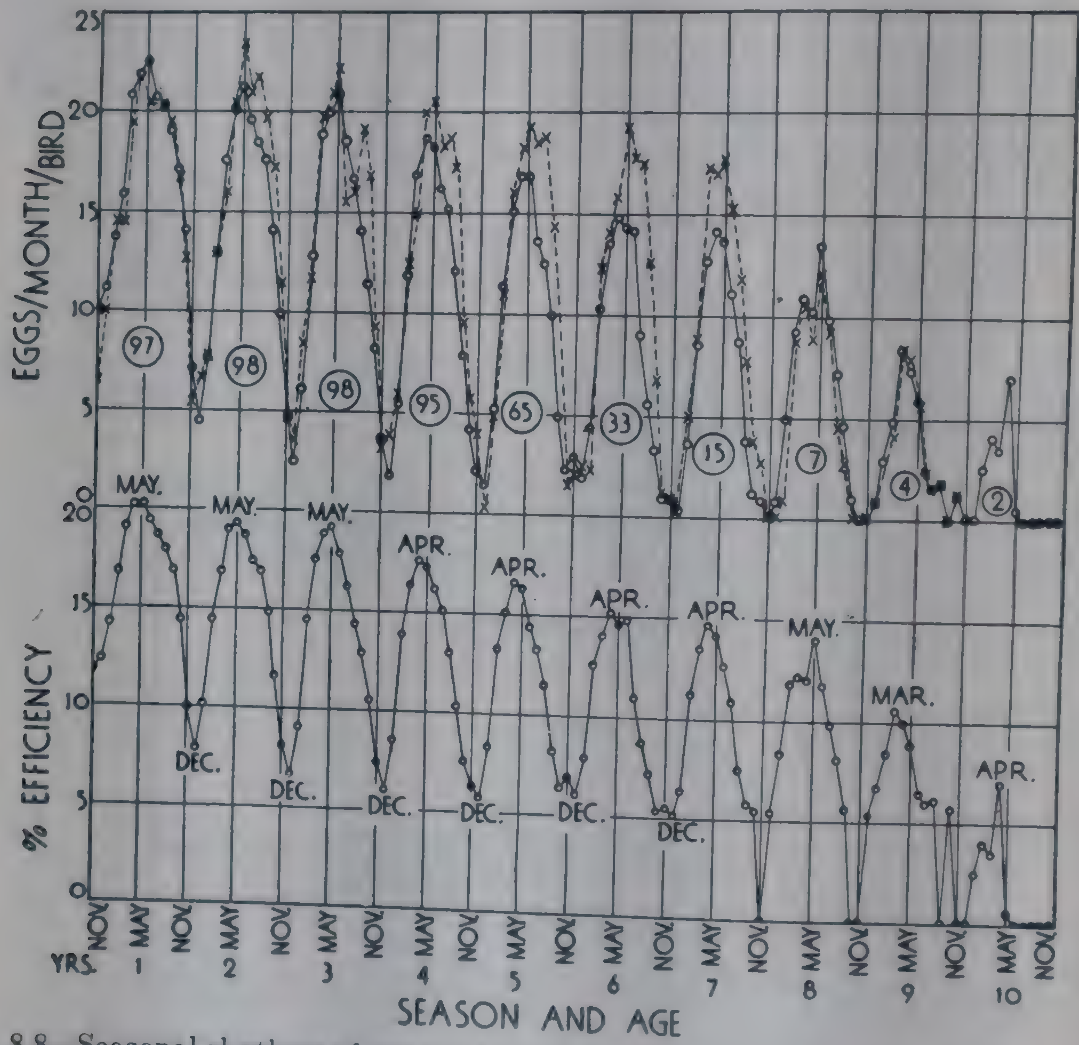

Fig. 8.8—Seasonal rhythms of egg production in chickens with increasing age, plotted from Brody, Kempster and Funk, Mo. Res. Bull. 278, 1938. The numerals in circles represent the number of original survivors in successive years. The circles represent all the birds under observation at successive years; the X's represent the same birds which produced for full 9 years.

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[61] For the photoperiodicity of goats see Bissonnette, *Physiol. Zool.*, **14**, 379 (1941).

As far back as 1909 Eckles[62], from the Missouri Station, made it generally known that the milk solids (especially butter fat, which determines the commercial value per unit milk) vary inversely with the milk-production level; consequently, the solids percentage in milk (except for vitamins and electrolytes) also shows a seasonal rhythm with a minimum in spring, when milk production is maximum, and maximum in winter when milk production is minimum (Fig. 8.9A to C).

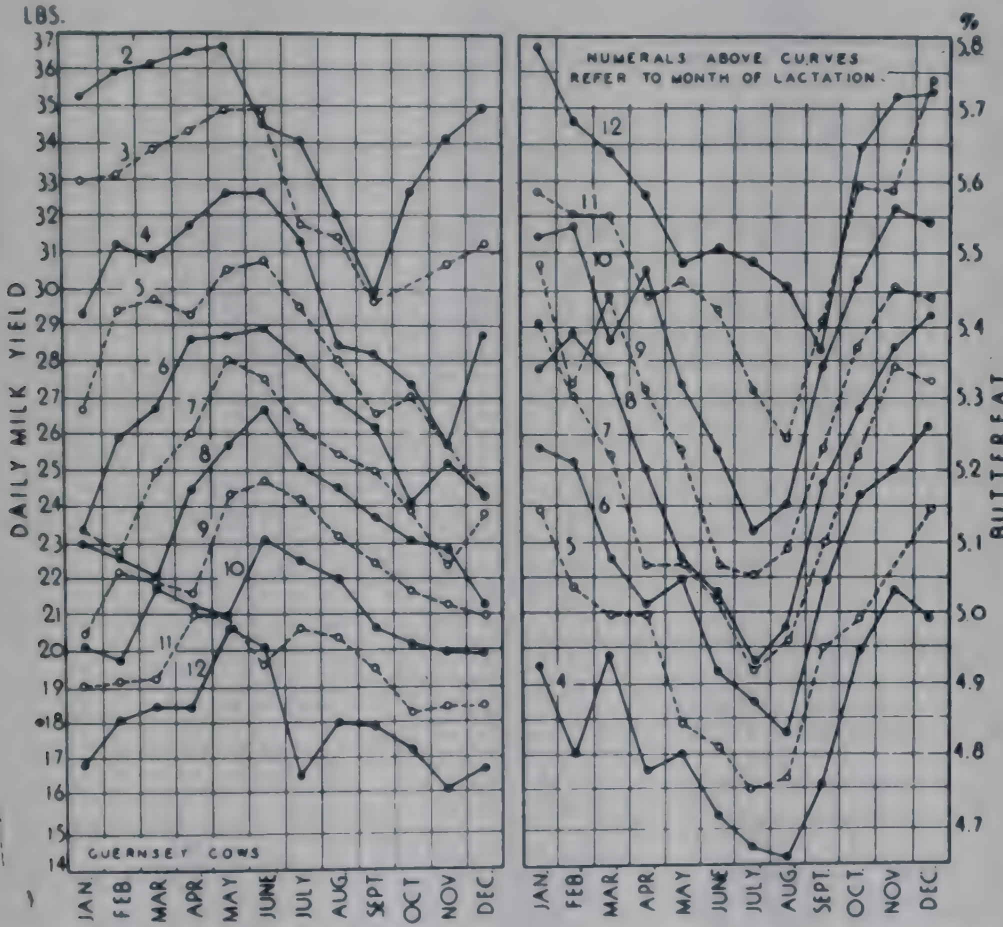

Fig. 8.9a—Seasonal rhythms in milk production. The charts are self-explanatory. The data compiled from various sources were tabulated in Univ. Missouri Agr. Exp. Sta. Res. Buls. 96 and 105. Several references including Sherman's data for sugar are given in the text. Note that milk yield tends to be maximal in May. When milk yield rises, left axis in 8.9a, fat per cent and other solids tend to decline, right axis in 8.9a. The maximal yearly yield is obtained when calving in autumn (Fig. 8.10b).

The month of calving exerts considerable influence on the persistency of the milk flow. It is usually more persistent in dairy cattle calving in the autumn, because when the flow would normally decline, about six months after calving, it gets a lift from the spring pasture and from the other favorable conditions associated with spring.

The month of calving tends to exert a similar influence on the maximum annual milk production as on the maximum persistency: calving in late autumn tends to yield the highest annual production, as shown in Fig. 8.10b.

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[62] Eckles, C. H., "Jahreszeitliche Schwankungen des Prozentischen Fettgehaltes in Kuhmilch," *Milchwirtschaftliches Zentralbl.*, **5**, 448 (1909).

The literature is not, however, fully consistent[63] on this point; it depends, no doubt, on the locality in which the data are obtained.

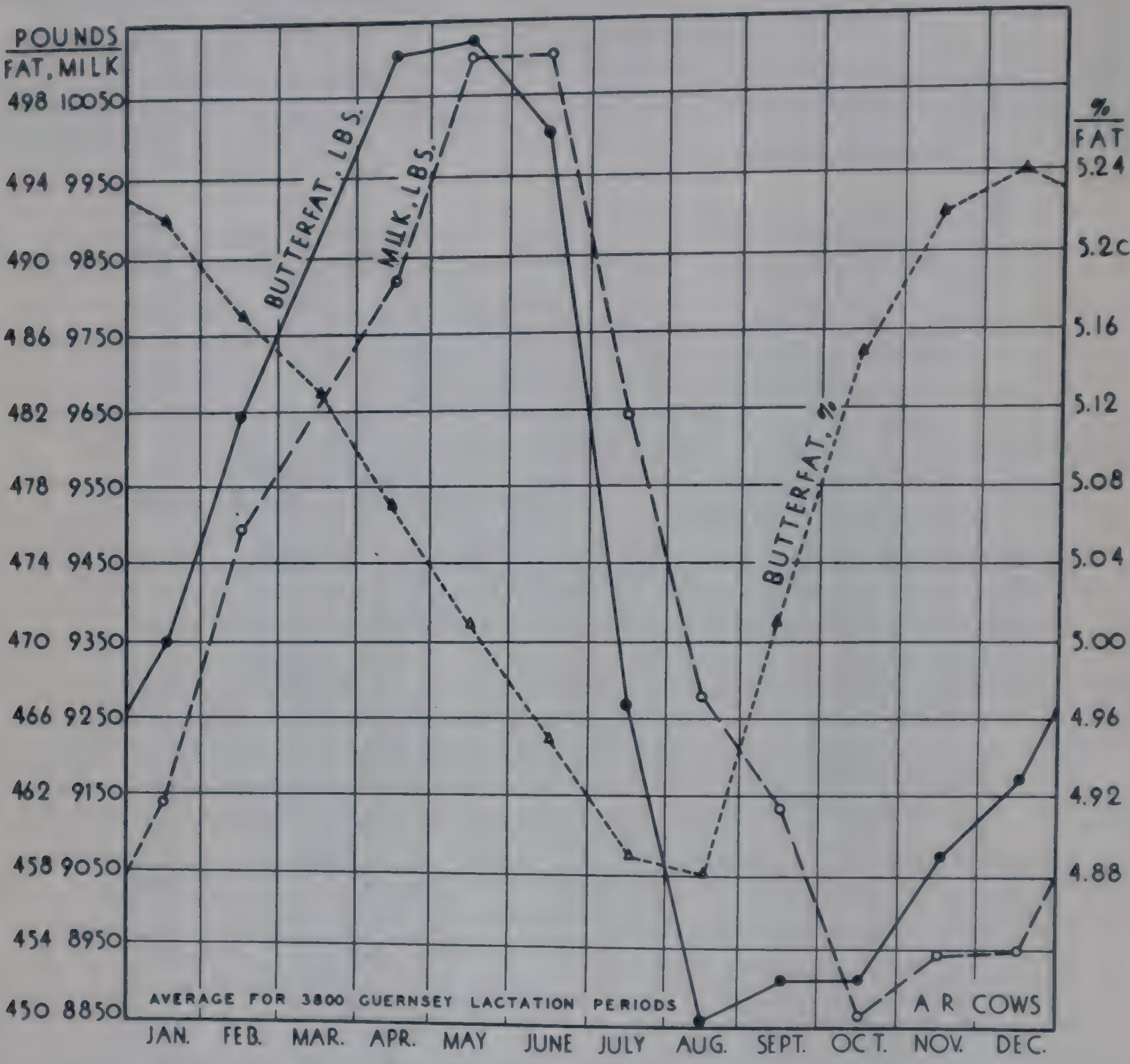

Fig. 8.9b—See legend 8.9a.

8.6: Seasonal growth and metabolic rhythms. The seasonal rhythm in food supply, sunshine, and warmth should influence the rates of growth and metabolism, which they do.

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[63] References to seasonal rhythms in milk production: Sherman, H. C., *J. Am. Chem. Soc.*, **28,** 1719 (1906); White, G. C., and Judkins, H. F., Storrs Agr. Exp. Sta. Bull. **94,** 1918; Clothier, R. W., Proc. 39th Meet. Soc. Promotion Agric. Sci. 1919; Ragsdale, A. C., and Turner, C. W., *J. Dairy Sci.*, **22,** 1922; Ragsdale, A. C., and Brody, S., *Id.*, **5,** 212 (1922); Ragsdale, A. C., and Turner, C. W., *Id.*, **5,** 544 (1922); Wylie, C. E., *Id.*, **8,** 127 (1925); Hays, W. P., *Id.*, **9,** 219 (1926); Brooks, H. J., *Id.*, **14,** 483 (1931); Cannon, C. Y., *Id.*, **16,** 11 (1933). Headley, F. B., Nevada Agr. Exp. Sta. Bull. 131, 1933; Weaver, E., and Matthews, C. A., Iowa Agr. Exp. Sta. Res. Bull. 107, 1928; Bartlett, S., *J. Agr. Sci.*, **19,** 36 (1929); Campbell, K. W. D., *Id.*, **21,** 167 (1931); Bartlett, S., Golding, J., and Wagstaff, *Agr. Progress*, **9,** 95 (1932); Turner, C. W., Univ. Missouri Agr. Exp. Sta. Bull. 365, 1936; Gaines, W. L., *J. Dairy Sci.*, **10,** 117 (1927); and Ill. Agr. Exp. Sta. Bull. 288, 1927; Hammond, J., and Sanders, H. G., *J. Agr. Sci.*, **13,** Part I, 1923; Sanders, H. G., *J. Agr. Sci.*, **13,** Part II, 1923; **17,** 339, 502 (1927); **18,** 46, 209 (1928), and many others.

We shall not attempt to review the literature on seasonal growth rhythms (Palmer[64] and McKay[64] discuss the literature) but list[64] illustrative references and quote one chart on seasonal growth of children by Palmer, Fig. 8.11.

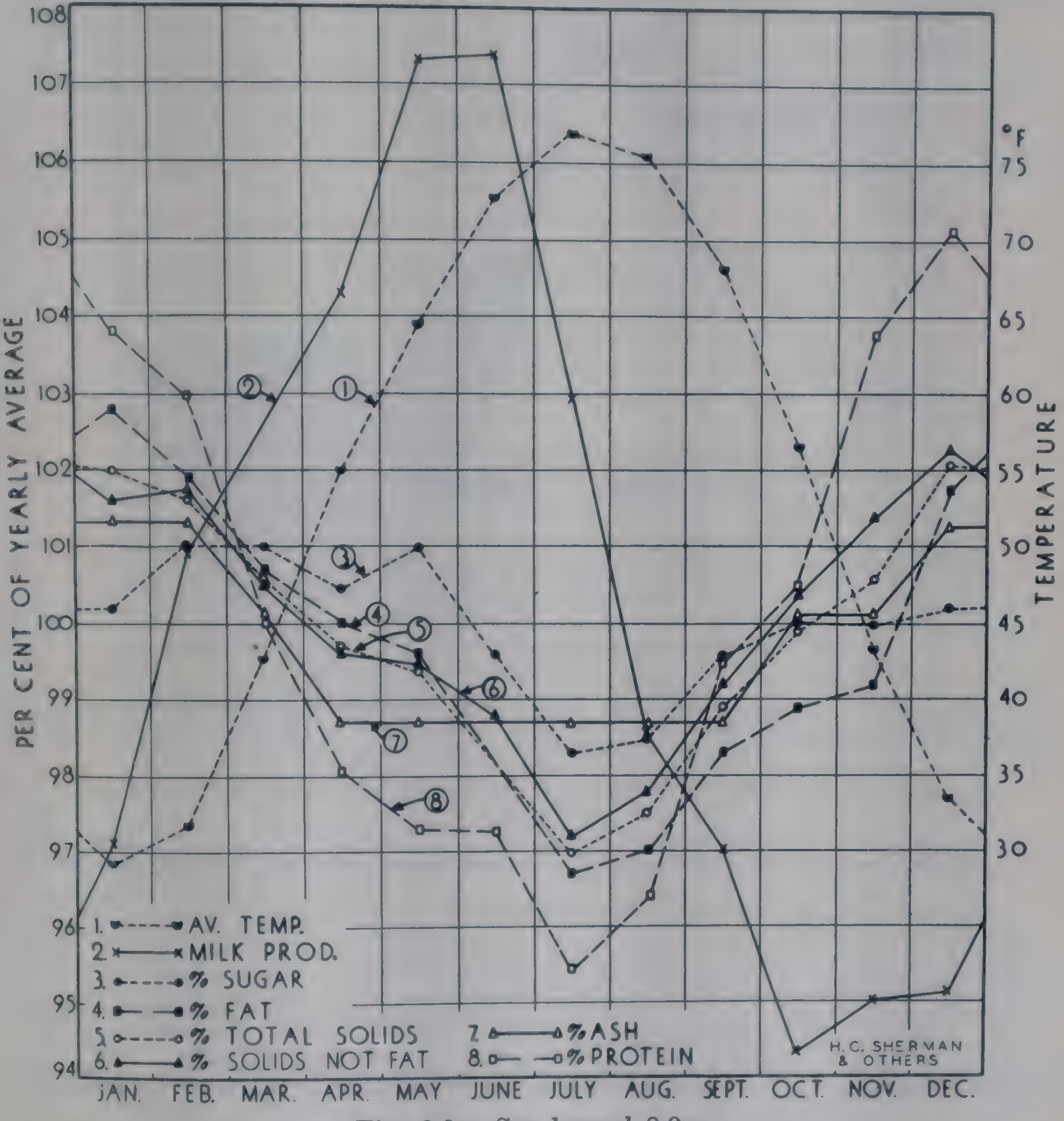

Fig. 8.9c—See legend 8.9a.

There is, as usual, considerable disagreement in detail; but the facts appear to be that weight growth in children tends to be most rapid (about 1 pound

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[64] Malling-Hansen, R., "Daily weighing of 1300 pupils of the Royal Institution for the deaf and dumb at Copenhagen," Congrés International des Sciences médicales. Copenhagen. 1884, and *Arch. Kinderheilk*, **13**, 84 (1891). Schmid-Monnard, *Jahrb. kinderheilk. u. phys. erziehung.*, **40**, 84 (1895). Palmer, C. E., *Public Health Reports*, **48**, 211 (March 3, 1933). Orr, J. B., and Clark, M. L., *Lancet*, II, No. 5581, 365 (1930). Berkson, J., *Human Biology*, **2**, 523 (1930); McKay, H., and Brown, M. A., Ohio Agr. Exp. Sta. Bull. 482, 1931; Emerson, H., *J.A.M.A.*, **89**, 1326 (1927). Nylin, G., *Acta Medica Scandinavica*, (suppl) p. 31, 1929. Porter, W. T., *Am. J. Physiol.*, **52**, 121 (1920). Bleyer, A., *Arch. Ped.*, **34**, 366 (1917). Brugsch, T., *Arch. mikroskopische Anat.*, **94**, 500 (1920). Frank, H., *Arch. Kinderheilk.*, **75**, 1 (1925). Louche, A., *Centralb. allg. path. pathol. anat.*, **36**, 481 (1925).

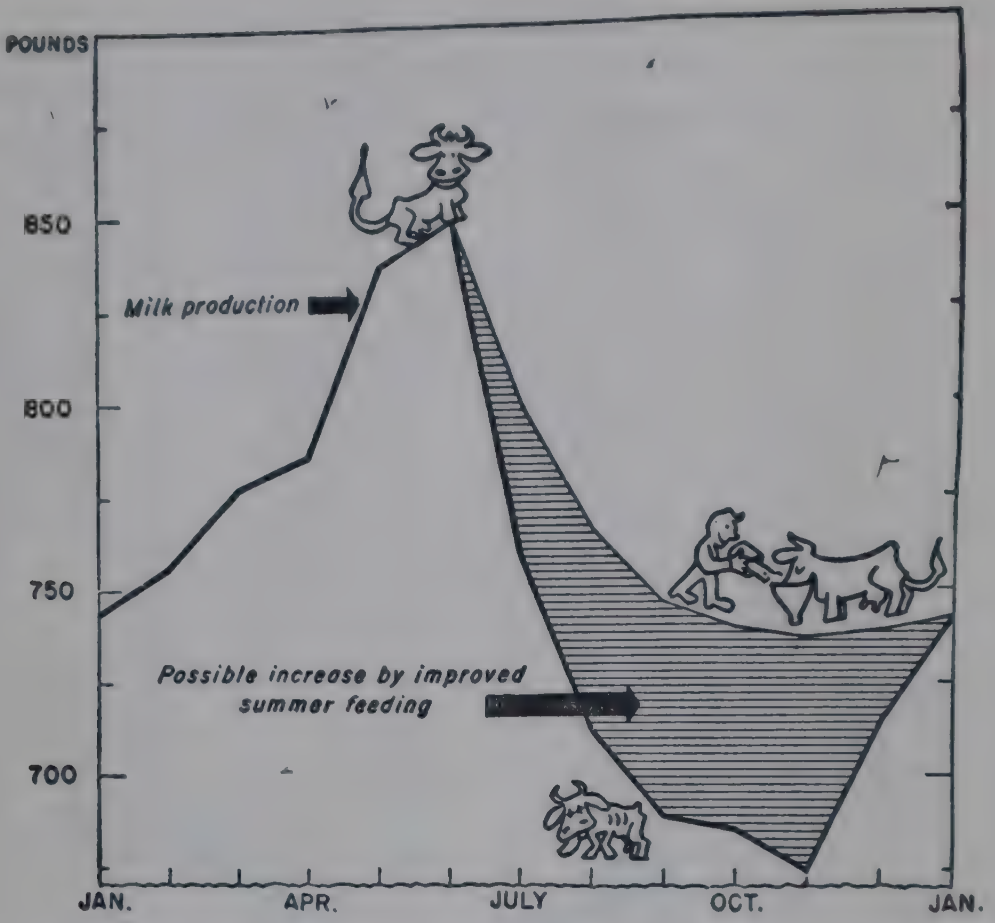

Fig. 8.10a—From a 1943 educational leaflet of the U. S. D. Agriculture on the seasonal rhythm in milk production.

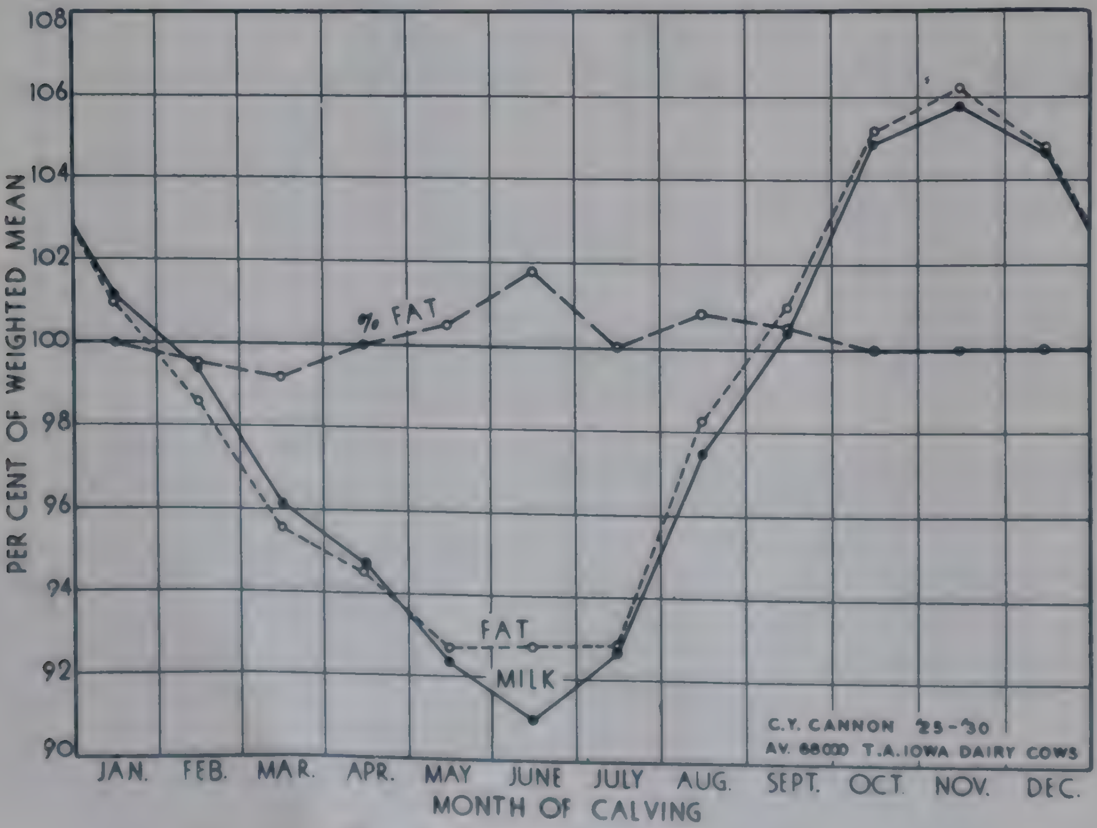

Fig. 8.10b—See legend 8.9a.

per month) during autumn (September to November in northern latitudes, and April to June in southern latitudes); and least rapid (about ¼ pound per month) in the spring. (See Fig. 11.19 for an apparently seasonal growth rhythm in chickens, which is, however, a temperature effect.) There is also literature on annual energy-metabolism rhythms[65].

There are difficulties in interpreting seasonal metabolic data because factors other than season as such (*i.e.*, length of day, angle of the sun's rays, temperature, and related cosmic[66] influences) confuse the picture. Gestation and lactation, for example, as well as differences in feed supply and temperature are confusing factors in interpreting our seasonal goat data.

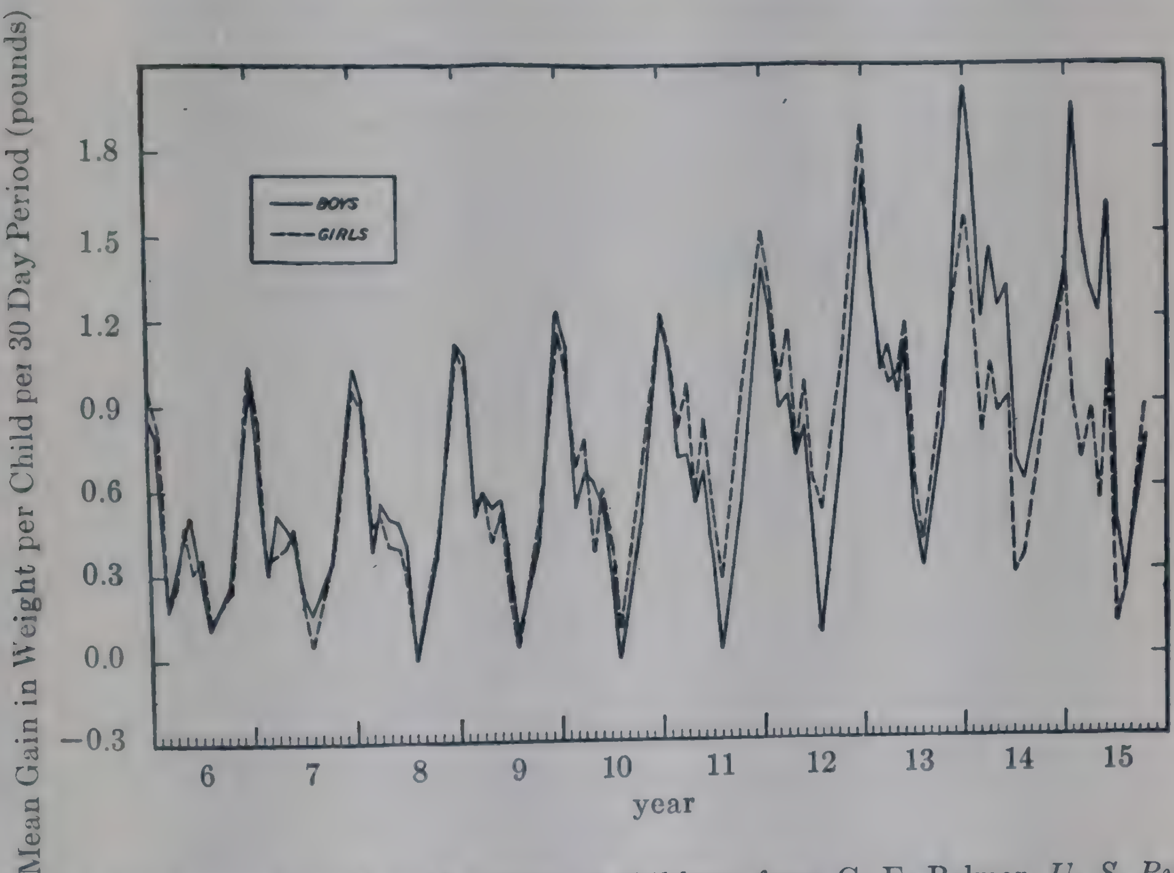

Fig. 8.11—Seasonal rhythm of growth of children, from C. E. Palmer, *U. S. Public Health Reports*, **48**, 211, 1933. Reprint 1561.

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[65] *Cf. inter alia*, Smith, E., "Experimental inquiries into the chemical and other phenomena of respiration, and their modifications by various physical agencies," *Phil. Trans.* p. 681, (1859) Maignon, F., et Guilhon, J., "Influence des saisons sur les combustions respiratoires chez le chien," Compt. Rend. Acad. Sci., **192**, 1410 (1931). Riddle, O., and Braucher, P. F., "Seasonal hemoglobin in doves," *Am. J. Physiol.*, **108**, 554 (1934). Riddle, O., Smith, G. C., and Benedict, F. G., "Seasonal endocrine and temperature factors which determine percentage metabolism change per degree temperature change," *Id.*, **101**, 88 (1932). Dontcheff, L., et Kayser, C., "Le rhythme saisonnier du métabolisme de base chez le pigeon," *Ann. Physiol. physicochim. biol.*, **10**, 285 (1934). Mayer, A., et Nichita, G., "Variation saisonnier du métabolisme du lapin," *Id.*, **5**, (1929). Lindhard, J., "Seasonal respiration periodicity," *Skand. Arch. Physiol.*, **26**, 221 (1912).

[66] *Cf.* Arrhenius, S., "Die Einwirkung kosmischer Einflusse auf physiologische Verhältnisse," *Skand. Arch. f. Physiol.*, **8**, 367 (1898).

With these difficulties in mind, let us discuss briefly the interrelations between the metabolic (energy metabolism) and breeding rhythms. As regards energy-metabolism rhythms in humans, Gustafson and Benedict[67] found no significant rhythm in body temperature, "but the average values for the oxygen consumption strongly suggest that the metabolism tends to be at a low level in the winter and to rise to a higher level during the spring and summer."

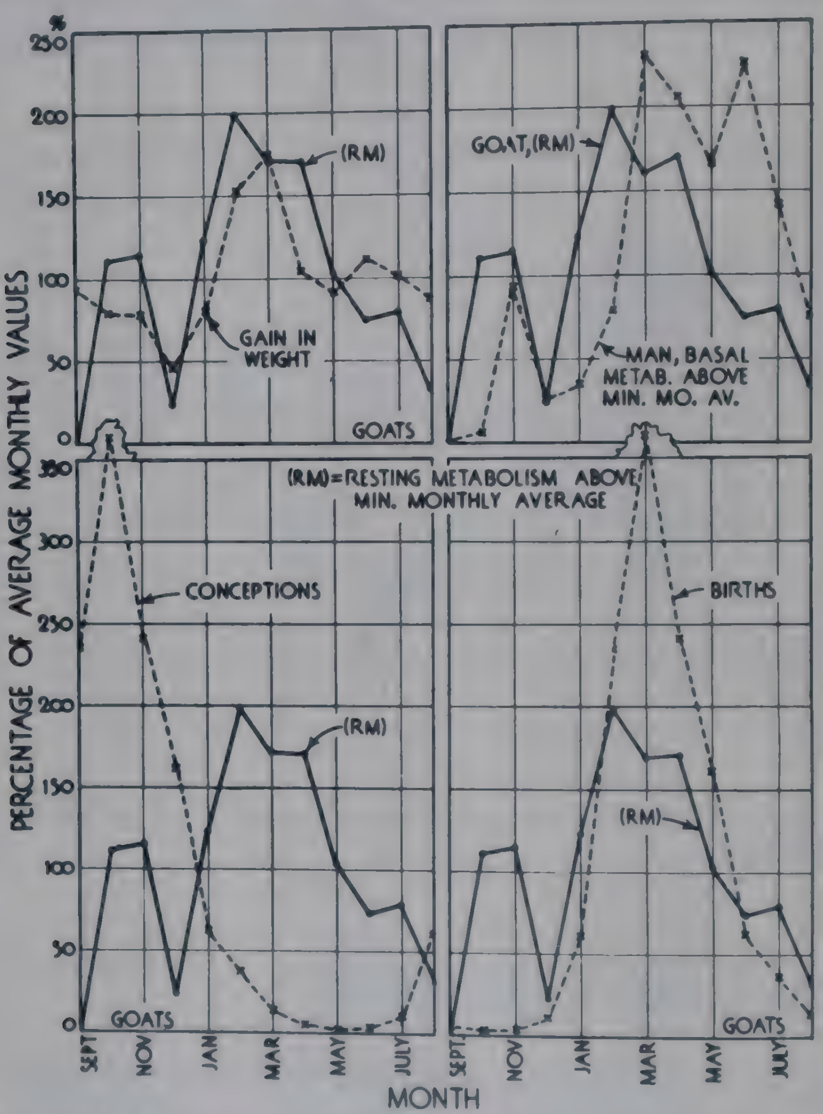

Fig. 8.12a—Seasonal rhythm in resting metabolism (R.M.) and of conception in goats (lower left), metabolism and birth in goats (lower right), metabolism and weight gains in goats (upper left) and resting metabolism (R.M.) in goats and basal metabolism in man (upper right).

We have investigated[68] the seasonal energy-metabolism and growth rhythms in goats and compared them with the seasonal breeding[69] rhythms. The results are shown in Fig. 8.12a. We also present in this chart the basal-energy metabolism data of humans kindly placed at our disposal by Professor Fred R. Griffith,[70] University of Buffalo. All the data were plotted in terms of percentages as follows.

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[67] Gustafson, F. L., and Benedict, F. G., "The seasonal variation in basal metabolism," *Am. J. Physiol.*, **86**, 43 (1928).

[68] Brody, Sandburg, and Asdell,[1] 1938.

[69] Asdell, S. A., *J. Agr. Sci.*, **16**, 632 (1926). Turner, C. W., *J. Dairy Sci.*, **19**, 619 (1936).

> The lowest average monthly metabolism was taken as base line. This base value was deducted from each monthly metabolism (average) and the differences were plotted against the corresponding months as percentages of the average monthly metabolism increment. Similarly, the monthly weight gains were plotted as percentages of the yearly average of the monthly weight gains and the monthly breeding frequencies. In this way the metabolism, growth, and sex activity rhythms become comparable.

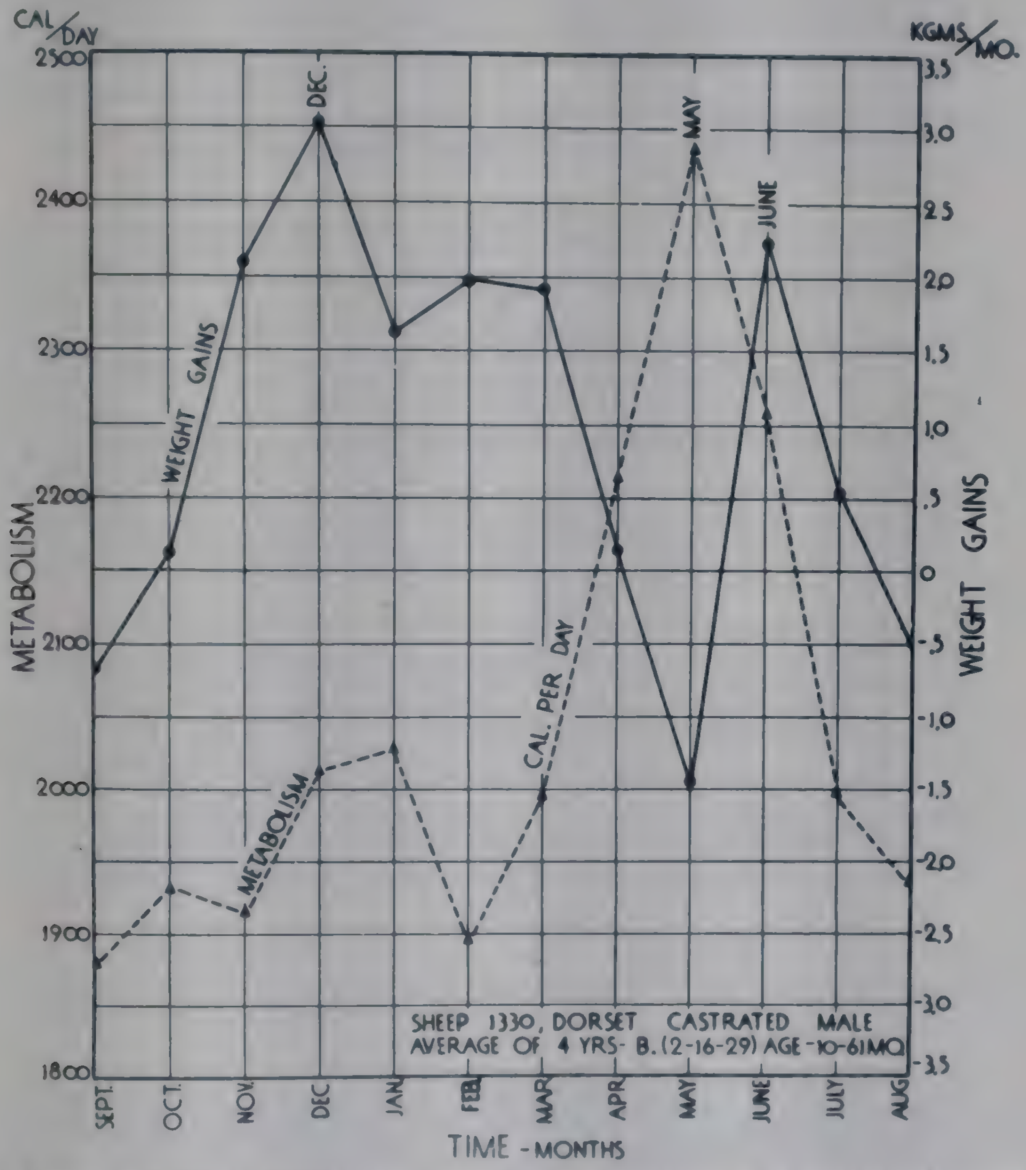

Fig. 8.12b Seasonal growth and metabolism rhythm of a castrated sheep.

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[70] *Cf. inter alia*, Griffith, F. R., Jr., and his associates: "I. Metabolism and oral temperature," *Am. J. Physiol.*, **87**, 602 (1929); "II. Pulse rate and blood pressure," *Id.*, **88**, 295 (1929); "III. Alveolar air and blood gas capacity," *Id.*, **89**, 449 (1929); "IV. Vital capacity, respiratory rate and volume, and composition of expired air," *Id.*, **89**, 555 (1929); "V. Urine Chemistry," *J. Nut.*, **5**, 131 (1934); "VI. Blood Chemistry," *Id.*, **6**, 169 (1934).

Fig. 8.12a shows that the metabolic peak in goats (as in sheep) occurs in early spring. The weight gains in growing goats are also maximum in early spring. The breeding peak, on the other hand, occurs in the autumn. The tentative conclusion, therefore, is that there is an inverse relationship between high breeding level and high energy-metabolism level.

We plotted Griffith's human data on the upper right corner of Fig. 8.12a as we did our goat data, in terms of percentages of average annual metabolism increment above the base level. The time curve of metabolism of humans is similar to that of the goat in spite of the fact that humans do not have an annual sex rhythm in temperate zones. Fig. 8.12b represents the seasonal rhythms in a castrated sheep, with a spring maximum.

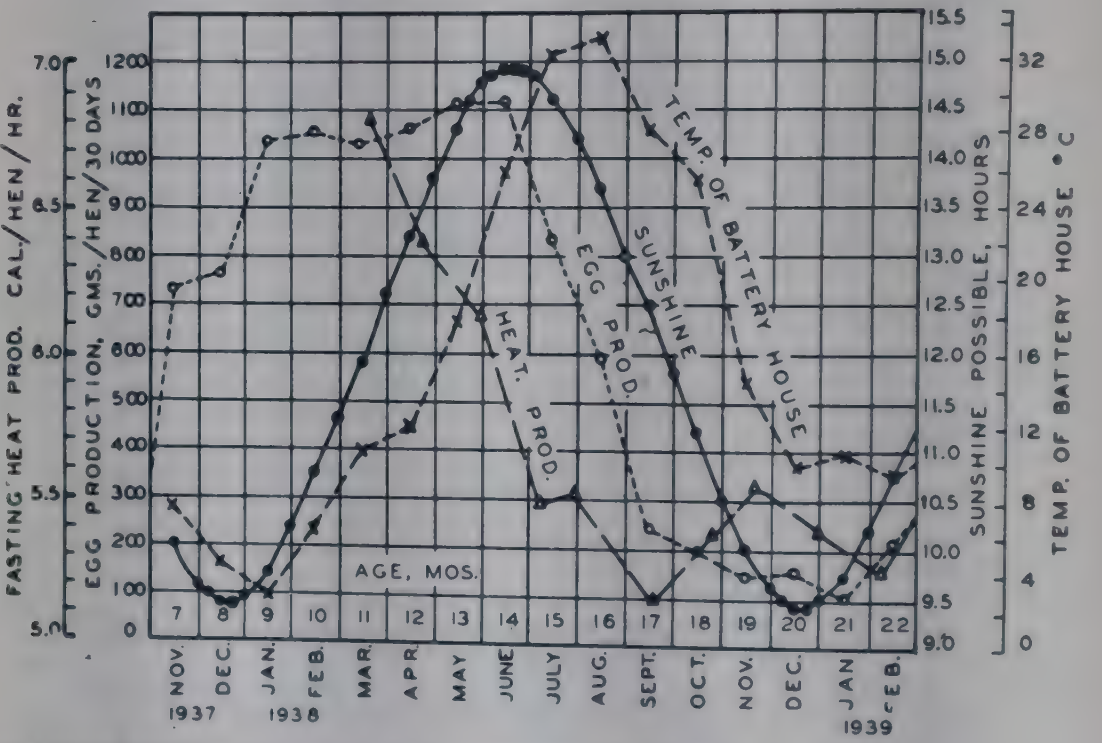

Fig. 8.13a—Seasonal metabolic and reproductive rhythms in the domestic fowl, also sun rhythm in Columbia, Mo.

We have also investigated the seasonal rhythm of basal heat production in domestic fowl[71] (Fig. 8.13a) which indicates a parallelism between basal metabolism and egg production. This does not mean that a high reproduction rate as such is associated with a high metabolism rate. The high basal metabolism during high egg production in the fowl may reflect the massive energy transformations associated with egg production rather than with primary reproductive activity. As shown in Fig. 8.12a, the peak metabolism in goats (R. M. = "resting" metabolism, 12 hours after feeding, which is not postabsorptive in this species) coincides not with maximum breeding activity, as in the fowl, but with minimum breeding activity. The seasonal rhythm in heat production is thus a problem in multiple causation rather than of simple cause and effect.

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[71] Winchester, C. F., Univ. Missouri Agr. Exp. Sta. Res. Bull. 315, 1940.

Many other rhythms might be cited, such as the seasonal rhythm of receptivity of the capon's comb to androgens reported by David[72] and by Laqueur[73]. Duszynska[74] reported that the response of castrated mice to estrone is three times as great in May as in November. It is evident that season influences the sensitivity of the receptive as well as of the "causative" organs.

One could discuss other seasonal rhythms, such as those of blood volume (Ch. 11, Bazett), hemoglobin concentration, calcium, phosphorus, blood fat, and blood coagulation (most rapid in the summer). In connection with Fitt's theory of spring instability mentioned in the beginning of this chapter, and Bazett's "torrents of spring" (Ch. 11), it is interesting to note that the suicide peak is maximum in spring (Fig. 8.14).

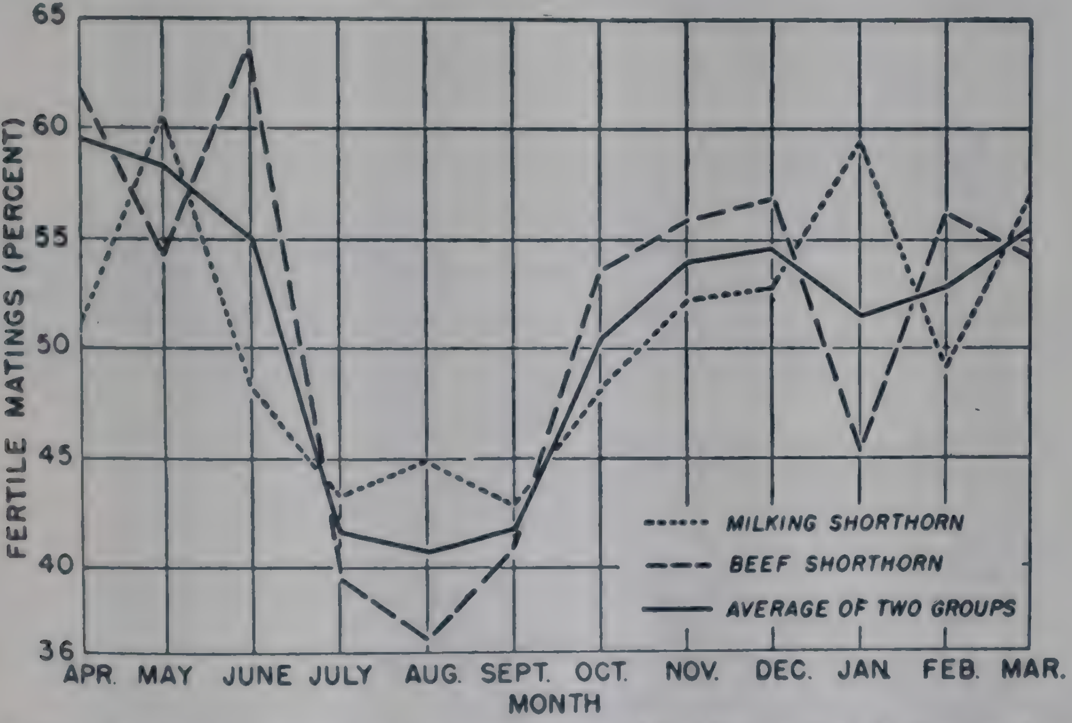

Fig. 8.13b—Seasonal changes in the percentage of fertile matings in beef and milking shorthorn bulls. Courtesy R. W. Phillips, B. Knapp, Jr., L. C. Heemstra and O. N. Eaton, *Am. J. Vet. Res.*, **4**, 115, 1943.

One could also discuss the seasonal hibernation-rhythm phenomena based on the marmot[75] (ground-hog) so famous for its weather-prognosticating abilities (on February 2 it is supposed to wake up, and if it sees its shadow, it promptly retires to its hibernation because of forthcoming cold weather within six weeks). During the summer its body temperature, pulse rate, and respiration rate are of the same order as of non-hibernating mammals of the same size. In autumn, however, when the environmental temperature drops to 50–60°F (10–15°C), and, incidentally, the food supply decreases, it goes into hibernation; its body temperature falls from the normal 37° to 30°C, to 15°C, and finally to 6°C, or even 3°C (37° to 43°F). The pulse drops from the normal of 200 per minute to perhaps 4 to 5 per minute. Unlike cold-blooded animals, however, when the environmental temperature drops below 42°F (6°C), it wakes up, thus preventing it from freezing to death. These animals are thermo- rather than photoperiodic.

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[72] David, K., *Acta brevia Neerlandica*, **8**, 133 (1938).

[73] Laqueur, cited by Duszynska.[74]

[74] Duszynska, J., *Nature*, **142**, 673 (1938).

[75] Benedict, F. G., and Lee, R. C., "Hibernation and marmot physiology," Carnegie Institution of Washington, Publication 497, 1938. Johnson, G. E., "Hibernation in mammals," *Quart. Rev. Biol.*, **6**, 439 (1931). Rasmussen, A. T., *Am. Naturalist*, **1**, 609 (1916); *Endocrinology*, **5**, 33 (1921). (The hypophysis in the woodchuck with special reference to hibernation"). Herter, K., "Körpertemperatur und Aktivität beim Igel," *Z. vergl. Physiol.*, **20**, 511 (1934).

8.7: Summary. Many species are photoperiodic. Domestication under special conditions of food supply tends to disturb this photoperiodism. This modification of the breeding pattern may be due to an interrelation between the feed supply and sunlight, perhaps similar to the interrelation between sunlight and dietary vitamin D, calcium and phosphorus salts.

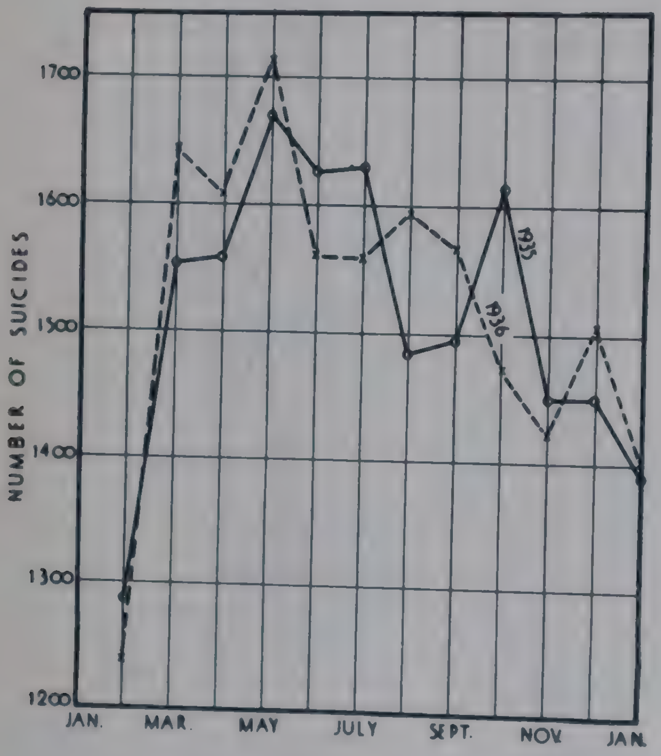

Fig. 8.14—Seasonal suicide rhythm in the United States (plotted from U. S. Bureau of Census, Vital Statistics Special Reports, Vol. 3, No. 11, p. 67, April, 1937, and Vol. 5, No. 20, p. 55, March 1938. Not indicated by sex).

On the other hand, many domestic species are decidedly seasonal in their breeding pattern, perhaps dependent on the seasonal light pattern.

The seasonal metabolic rhythms parallel the reproductive rhythm in the fowl (spring peak, Fig. 8.13a), but not in the goat (conception peak in autumn, metabolic peak in spring, Fig. 8.12a). The metabolic rhythm parallels the growth rhythm in the goat (spring peak, Fig. 8.12a), but not in man (metabolic peak in spring, Fig. 8.12a, growth peak in autumn, Fig. 8.11).

The breeding season is timed so that the young will be born during the most favorable time; hence the breeding time is related to the length of the gestation period, to the environmental temperature, and to food supply, all of which are in turn related to sunlight. Hence the tremendous species differences in sensitivity to day length: some species are stimulated to sex activity by shortening days, others by lengthening days. Still others are apparently unaffected by day length.

The anterior pituitary is thought to be involved in photoperiodic gonadal activity. It is assumed that light falling on the eye stimulates (by nervous channels) the pituitary to produce gonadotropic hormone. Thyroid activity, which is sensitive to changes in temperature and light irradiation, may be an influencing factor.

While sudden changes in day length may induce sex activity, they may not result in increased fertility because of premature and abnormal maturation of the sex cells, and because of high mortality. For normal breeding out of season, graduated changes in day length simulating the natural seasonal changes in day length may be required. There is an obvious need to investigate these phenomena as they relate to farm animals and thus to learn to control their timing.

Chapter 9

Metabolic Catalysts in the Efficiency Complex: Diurnal Rhythms

> Science started with the organization of ordinary experience. *A. N. Whitehead*

9.1: Introduction. We became interested in the problem of diurnal rhythm when we obtained some unexpected results in a study[1] of the heat increment of feeding (*SDA*, Ch. 4) of the rat. The anomalous result could be explained only by assuming the presence of a diurnal metabolic rhythm in which the difference between crest and trough exceeded the *SDA* effect of the feed (Fig. 9.1). This led to the performance of a series of experiments, and the discovery of a profound (25–30 per cent difference) diurnal metabolic rhythm in the rat which is not extinguished by a month of continuous light *alone*, by a month of continuous feeding *alone* ($\frac{1}{8}$ of the day's maintenance ration at 3-hour intervals), nor by a combination of continuous light and fast. It is extinguished, however, by a week of continuous light *and* continuous feeding. The object of this chapter is to summarize some of these results and integrate them with the literature on diurnal rhythms in general as a logical sequence to the preceding chapter on seasonal rhythms in general, with special reference to the efficiency complex.

There is an evident analogy between diurnal and seasonal rhythms, both being ultimately activated by the sun rhythm; and metabolic effects—however different in nature—are exerted not only on photosynthetic plants but also on animals endowed with visual or related extroceptive apparatus. The timing of the rhythmic activity in animals, whether they are diurnal or nocturnal, depends on the nature of their visual apparatus, whether they see best in bright light (day) or in dim light (night). The diurnal light rhythm, through the intermediacy of the amplifying visual apparatus, exerts a profound effect on all life processes. Sleep is a conspicuous illustration; so are there rhythms in body temperature and nervous irritability which are interrelated with muscular activity, with energy metabolism, with food intake, and so on. It seems instructive to review the literature in some detail so as to get a view of the situation as a whole.

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[1] Herring, V., and Brody, S., "Diurnal metabolic and activity rhythms," Univ. Missouri Agr. Exp. Sta. Res. Bull., 274, 1938.

9.2: The literature. When travelling, the *body temperature* rhythm follows the light rhythm[2]. In man, the average minimum daily temperature, 36.5° C, is in the early morning (2 to 5 a.m.) and the maximum, 37.5° C, in the afternoon (2 to 5 p.m.). In the pigeon[3] the midnight temperature, 41.5° C, is below the noon temperature, 42.2° C.

The most dramatic feature of the diurnal rhythm is *sleep*. Kleitman[4] gave a good description of its natural history in man (1929).

> "Darkness makes for poor vision and discourages movements. This leads to inactivity and relaxation, and sleep follows. Repeating the performance a great many times results in the establishment of a conditioned reflex of a temporal character, relaxation at a certain time. This is the theoretical history of diurnal sleep.
>
> "Practically we are born into a social organization where diurnal sleep is the uni-

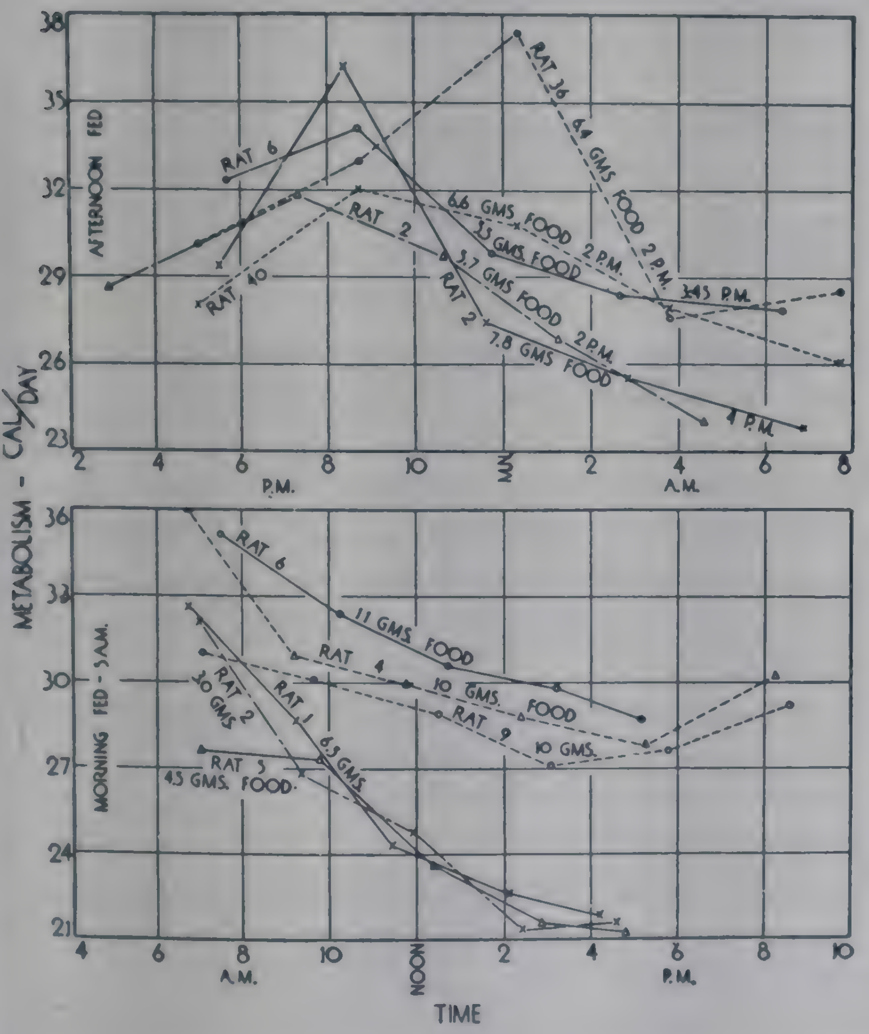

Fig. 9.1. Apparent difference in heat increment of feeding in rats following morning and afternoon feeding.

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[2] Gibson, R. B., "Body temperature periodicity," *J. Med. Sci.*, **129**, 1048 (1905). Osborne, W. A., *J. Physiol.*, **36**, p. XXIX-XLI (1908).

[3] Burckard E., Dontcheff, L., *et* Kayser, C., "Le rythme nycthérméral chez le pigeon," *Ann. physiol. physicochim. biol.*, **9**, 303 (1933). For other body temperature rhythms see Simpson, S., and Galbraith, J. J., "Body temperature variations of nocturnal and other birds, and mammals," *J. Physiol.*, **33**, 225 (1905); Wetmore, A., "A study of the body temperature of birds," *Smithsonian Misc. Coll.*, **72**, 1 (1921).

[4] Kleitman, N., "Sleep," *Physiol. Rev.*, **9**, 624 (1929). "Sleep and wakefulness," Univ. Chicago Press, 1939.

versally accepted mode of sleeping. The first habit that a mother tries to develop in a baby is that of an unbroken night's sleep. As he gets older other functions develop a periodicity that coincides with the enforced sleep periodicity. For instance, a temperature curve develops with a minimum at night, and produces a disinclination to night activity. Even the modest tear apparatus stops its function at bedtime procuring dry eyes, favoring their closure."

Nervous irritability follows a similar rhythm. The reaction of normal man to light and sounds is lowest in the morning, when body temperature is lowest, and increases with increasing body temperature in the afternoon, then returns to the morning minimum. When the body temperature is at a minimum, irritability is likewise at a minimum, and it is then most difficult to keep awake. Skills of coordination are at a minimum during these early hours[5].

The influence of nervous irritability on metabolism and body temperature may be inferred from the facts that about half of the peripheral nerves supply the skeletal muscles and about half of the body mass is muscle. The increase of the contractions of skeletal muscle is proportional to the increase in nervous irritability[6].

The literature on the *development of activity rhythms* is somewhat conflicting. Thus Richter[7] reported that the rhythms gradually develop (first appear in rats about 12 days after birth), presumably because of social conditioning. Barott[8], on the other hand, reported that the metabolic rhythms "decrease rapidly with age" in young chicks. "At the average age of 1 week . . . an average maximum difference of about 24 per cent was observed between the oxygen consumption at 8 a.m. and 8 p.m. values." (The peak occurred at 8 a.m. and the trough at 8 p.m.)

Richter[7] reported that the diurnal rhythmic activity of the fasting rat persisted even in the absence of light cycles. On fasting, during the early period of fast, the total activity was greater than during five previous feeding days. We found the same to be true.

The *feeding rhythms* naturally follow the activity rhythms, being usually confined to times when vision functions best, which is night for rats and other nocturnal animals and day for fowl and other diurnal animals. There are corresponding nutrition-function rhythms. Thus glycogen storage in rabbits, rats, and mice is maximal and bile formation is minimal during the night[9]. In nocturnal animals, the assimilatory phase when the glycogen s deposited occurs during the night when the animals naturally feed[10]. The glycogen deposition at this time tends to be counteracted, however, by physical activity; this occasionally results in a bimodal curve of glycogen storage.

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[5] Kleitman, N., Titelbaum, S., and Feivoson, P., "Diurnal variation in reaction time," *Am. J. Physiol.*, **113**, 82 (1935). Freeman, G. L., and Hovland, C. I., "Diurnal variations in performance," *Psychol. Bull.*, **31**, 777 (1934). Jores, A., "Die 24 Stunden-Periodik in der Biologie," *Tabulae Biologicae*, **14**, 77 (1937).

[6] Jacobson, E., "Variations in muscular tonus," *Am. J. Physiol.*, **113**, 71 (1935).

[7] Richter, C. P., *Comp. Psychol. Monographs*, **1**, 55 (1922); *Quart. Rev. Biol.*, **2**, 307 (1927).

[8] Barott, H. G., Fritz, J. C., Pringle, E. M., and Titus, H. W., *J. Nut.*, **15**, 145 (1938).

[9] Agren, C., Wilander, O., and Jorpes, E., "Cyclic changes in the glycogen content of the liver and muscles of rats and mice," *Biochem. J.*, **25**, 777 (1931). Forsgren, E., *Skand. Arch. Physiol.*, **53**, 137 (1928), **55**, 144 (1929). *Acta. Med. Scand.*, **73**, 213 (1930).

In diurnal animals the blood-sugar and adrenaline peaks occur during the day (and the calcium peak at night), opposite to the liver glycogen peak[11]. Incidentally, in diabetics the blood-sugar level falls during the evening, often below the fasting level[12]. Lactating cattle tend to exhibit blood-sugar rhythms[13]. The trend is likely to be confused because of the sensitiveness of the blood-sugar level to psychic disturbances involved in securing the blood. (In lactating cows the blood-sugar level reached a high of 70 mg sugar per 100 cc blood at noon and a low of 58 mg at 9:30 a.m. There was no such trend in non-lactating cows or sheep.)

Diurnal rhythmicity was also reported for blood volume[14], non-protein nitrogen[15], serum calcium[16], red corpuscles and hemoglobin[17], water and minerals[18].

There is an apparent diurnal rhythm in the composition of milk[19] (Fig. 9.5). The diurnal difference in fat percentage is attributed to differences in time-interval between day and night milkings. Morning milk is richer in bacteria than evening milk, and evening milk is richer in chlorine and catalase than morning milk[20].

Domestic fowl lay eggs only during the day (7 a.m. to 5 p.m.)[21].

The "alkaline tide"[22] (urinary-acidity rhythm) is obviously associated with the diurnal feeding rhythm. The sensitiveness of urinary reaction to diet is indicated by the fact that ingestion of 5 g sodium biocarbonate results in an immediate rise in alkalinity of the urine. The urinary-volume rhythm tends to parallel the body-temperature rhythm[23]. The blood pH in humans rises from morning to late at night[24].

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[10] Higgins, G. M., Berkson, J., and Flock, E., *Am. J. Physiol.*, **102,** 673 (1932); **105,** 177 (1935).

[11] Euler, U. S., Holmquist, A., *Pflüger's Arch.*, **234,** 210 (1934). Holmquist, A., *Z. ges. exp. Med.*, **93,** 370 (1934).

[12] Mollerstrom, J., *Acta Med. Scand. Suppl.*, **50,** 250 (1937).

[13] Allcroft, W. M., *Biochem. J.*, **27,** 1827 (1933).

[14] Holmgren, H., *Acta Med. Scand. Suppl.*, **59,** 104 (1935). Mollerstrom, J., *Acta Med. Scand. Suppl.*, **50,** 250 (1932); **59,** 145 (1934).

[15] Forsgren, E., *Acta Med. Scand.*, **73,** 213 (1930).

[16] Ehrstrom, M. C., *Acta Med. Scand. Suppl.*, **59,** 97 (1934). Holmquist[11].

[17] Short, J. J., *J. Lab. Clin. Med.*, **20,** 708 (1935).

[18] Norn, M., *Scand. Arch. Physiol.*, **55,** 184 (1929).

[19] Bartlett, S., *J. Agr. Sci.*, **19,** 38 (1929).

[20] Wisconsin Bull., 439 (Ann. Rept.), p. 76, Dec. 1937.

[21] Warren, D. C., and Scott, H. M., *J. Exp. Zool.*, **74,** 137 (1936).

[22] Cf. Campbell, J. A., and Webster, T. A., "Urinary tides." *Biochem. J.*, **16,** 507 (1922). Fiske, C. H., *J. Biol. Chem.*, **49,** 171 (1921). Cohen, I., and Dodds, E. C., *J. Physiol.*, **59,** 259 (1924).

[23] Simpson, G. E., *J. Biol. Chem.*, **59,** 107 (1924); **84,** 393 (1929).

[24] Cullen, G., and Earle, I. P., *J. Biol. Chem.*, **83,** 545 (1929).

The stomach-activity rhythms are presumably associated with feeding habits. There is an extensive literature on this problem[25].

Many miscellaneous diurnal rhythms have been observed, such as the mitotic rhythm in human tissue[26], spermatogenic rhythm in the sparrow[27], enamel deposit rhythm in the rat[28], retinal rhythm in catfish[29], brain-potential rhythms[30], cell-division rhythm in the thyroid[31], and so on.

According to Szymanski[32], in addition to diurnal rhythmicity, some species are *polyphasic*, exhibiting several periods of activity and rest during the day; others are *monophasic*, exhibiting one prolonged period of activity followed by one of rest during each day. Rabbits are polyphasic, having 16 to 21 periods of activity alternating with rest; albino rats have 10 periods of activity concentrated, as in other nocturnal animals, at night; canaries are monophasic, active during day and quiet during night; young dogs exhibit 8–13 periods of activity at night; cats exhibit ⅔ of their activity during the day, and ⅓ during the earlier part of night; human infants are polyphasic, human adults monophasic, with the aged resembling infants in being polyphasic. There are obvious difficulties in differentiating between such inherent phasic rhythms and merely spurious movements.

We are mostly interested in the energy-metabolism rhythms, which reflect all the others.

Lusk[32a] quotes the following table from Johansson on the diurnal rhythm of CO_2 production in man:

	Night CO_2	Day CO_2	Author
Complete muscular rest	100	105	Johansson
Ordinary rest in bed	100	110	"
Ordinary life (no hard work)	100	142	Tigerstedt
" " " " "	100	128	Pettenkofer and Voit
" " " " "	100	147	Tigerstedt

Benedict and Riddle[33] reported that muscular activity of pigeons in dark chambers is less during night than during day. After excluding the periods showing muscular activity, day metabolism was about 15 per cent above night metabolism.

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[25] See, among many others, Elliott and Bousfield, *Psychol. Rev.*, **43,** 94 (1936). Hellebrandt, F. A., *et al.*, *Am. J. Dig. Dis. and Nut.*, **3,** 477 (1936); Kleitman, N., *et al.*, *Proc. Am. J. Physiol.*, **116** (1936); Richter, *Quart. Rev. Biol.*, **2,** 307 (1927); Boldyreff, W., *Quart. J. Exp. Physiol.*, **10,** 175 (1916–17).

[26] Charleton, A., *J. Anat.*, **68,** 251 (1938); *J. Am. Med. Assn.*, **12,** 436 (1939).

[27] Riley, G. M., *Anat. Rec.*, **64,** Supp. 41 (1936); *Anat. Rec.*, **67,** 327 (1937).

[28] Steadman, S. R., *Anat. Rec.*, **63,** 325 (1935).

[29] Welsh, J. H., and Osborn, C. M., *J. Comp. Neurology*, 1937.

[30] Davis, H., Davis, P. A., Loomis, A. L., Harvey, E. H., and Hobart, C., "Human Brain potentials during the onset of sleep," *J. Neurophysiology*, **1** (1938). See several papers in *Cold Spring Harbor Symposia on Quantitative Biology*, **4** (1936).

[31] Cooper, Z., and Schiff, A., *Proc. Soc. Exp. Biol. Med.*, **39,** 323 (1930).

[32] Szymanski, J. S., *Pflüger's Arch. ges. Physiol.*, **6,** 136 (1895).

[32a] Lusk, G., "Science of Nutrition," Saunders, 1928.

[33] Benedict, F. G., and Riddle, O., "The measurement of the heat production in pigeons," *J. Nut.*, **1,** 475 (1929).

The pigeon was reported to have a 15 per cent diurnal basal metabolism and a 1° C rectal-temperature rhythm[34]. The fowl was reported to have a 30 per cent basal metabolism and a 1° C rectal-temperature rhythm[35]. The following (slightly rounded) data on rectal temperatures in fowl from Heywang[36] are illustrative of the course of the rhythm.

Time	8 a.m.	10 a.m.	12 noon	2 p.m.	4 p.m.	6 p.m.	8 p.m.	10 p.m.	12 night	2 a.m.	4 a.m.	6 a.m.	8 a.m.
Rectal temp. (°F)	106.8	106.5	106.4	106.4	106.8	106.8	105.9	105.5	105.4	105.6	105.9	106.3	106.5
Environmental temp. (°F)	53	68	74	79	76	64	56	50	48	46	44	42	54

Note that the environmental temperature happened to be changing at the same time, and Heywang suggested that there might have been a causal or dependent relation between rectal and environmental temperature. Of course, all aspects are interrelated, but it appears from other data that, in the main, the rectal-temperature *rhythm* would not have decreased appreciably if the environmental temperature had been kept constant at the mean value of about 60° F.

Kayser[34] demonstrated that the diurnal metabolic rhythm in the pigeon is due to the diurnal variation in tonicity of posture, especially of the pectoral muscles, which in turn is caused reflexly by the excitation produced by the diurnal light rhythm upon the nerves controlling muscle-tone.

Several reports are available on the inversion of body temperature obtained in animals by changing the light rhythm. This was accomplished on monkeys[37] and birds[38] in about 15 days. The results in inversion of body temperature and metabolism on man, however, are conflicting[39], because it is difficult to isolate him psychically and intellectually from the social rhythm of the environment even though he is isolated from the light rhythm.

The persistence of the diurnal rhythm in spite of prolonged rest and fast stimulated speculations on cosmic influences other than the sun, including cosmic rays and ionized air[40]. Deighton[41] observed a diurnal rhythm in metabolism of swine screened from changes in electrical conductivity. As previously noted, the thyroid, the prime metabolic regulator, has a diurnal growth (cell-division) rhythm.

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[34] Kayser, C., *et al.*[3]

[35] Bacq, Z. M., "Sur l'éxistence d'un rythme nycthérméral de metabolisme chez le coq," *Ann. physiol. physicochim. biol.*, **5**, 497 (1929). Terroine, E. F., "De l'éxistence d'un rythme nycthérméral de metabolisme chez les oiseaux," *Id.*, **5**, 842 (1929). Deighton, T., and Hutchinson, J. C. P., *J. Agr. Res.*, **30**, 140 (1940).

[36] Heywang, B. W., *Poultry Sci.*, **17**, 320 (1938).

[37] Galbraith, J. J., and Simpson, S., "Conditions influencing the diurnal wave in the temperature of the monkey," *J. Physiol.*, **20**, *Proc. Physiol. Soc.*, XX (1903).

[38] Galbraith and Simpson, *Id.*, **30**, XIX (1903). Hilden, A., and Stenback, K. S., *Skand. Arch. Physiol.*, **34**, 382 (1916).

[39] Benedict, F. G., *Am. J. Physiol.*, **11**, 145 (1904). Toulouse, E. F., and Pieron, H., *J. Physiol. path. gen.*, **9**, 245 (1907). Völker, H., *Pflüger's Arch. ges. Physiol.*, **215**, 43 (1926). Gessler, H., *Pflüger's Arch. ges. Physiol.*, **207**, 390 (1925).

[40] Völker, H., *Pflüger's Arch. ges. Physiol.*, **215**, 43 (1926).

[41] Deighton, T., *Physiol. Rev.*, **13**, 427 (1933).

9.3: Diurnal metabolic rhythm in the rat, its control and effect on the apparent SDA. The heat production per hour is the sum of: (1) the basal energy metabolism; (2) the energy expense of muscular activity and muscle tonus; and (3) the *SDA* (Ch. 4). As the rat is nocturnal, his muscular activity, nervous irritability, muscle tonus, feeding, and body temperature tend to be high during the night when his vision is best and low during the day when his vision is poorest. We may then expect high metabolic rates during the night and low metabolic rates during the day, just as Kayser found the opposite conditions in the pigeon. Our problems were: (1) to evaluate under our laboratory conditions the magnitude of the "normal" diurnal rhythm; (2) to investigate the conditions which may abolish the rhythm and thus obtain an insight into the mechanisms involved.

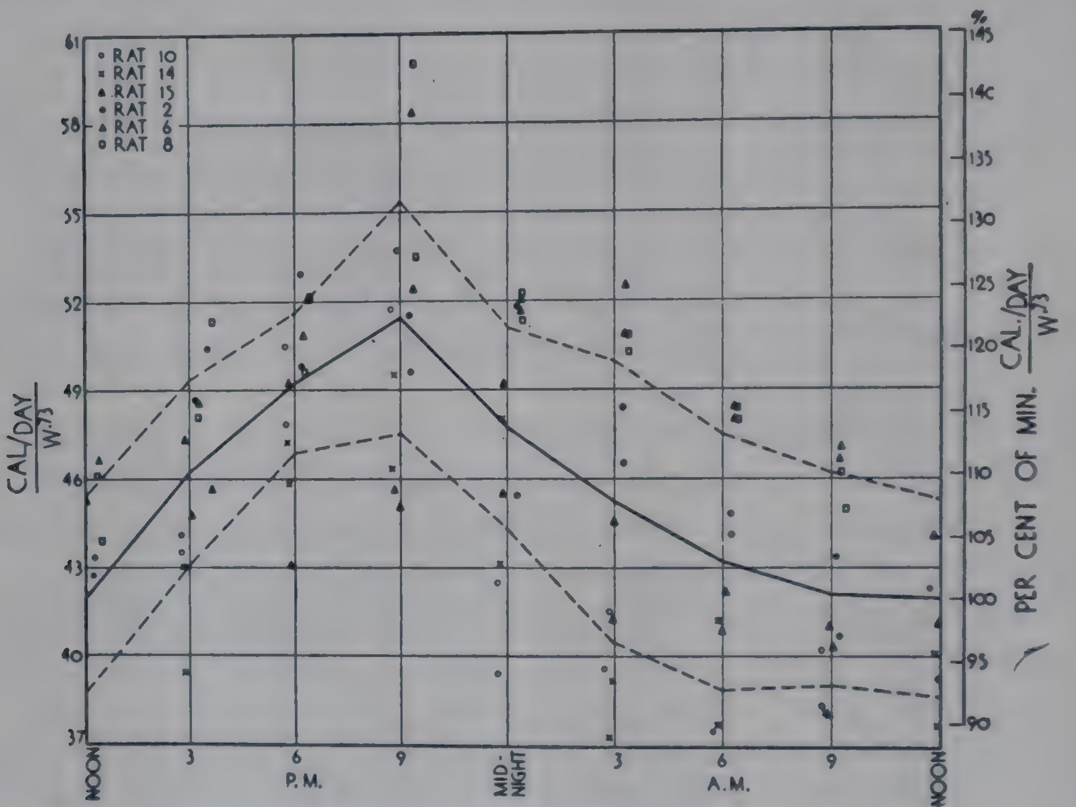

Fig. 9.2. The continuous line represents the avearge of the data for the 6 rats in Fig. 9.1. The area between the broken curves includes $\frac{2}{3}$ of the data.

The magnitude of the diurnal metabolic rhythm under "normal" conditions is shown in Figs. 9.1 to 9.3; there is 25 to 30 per cent difference between the peak and crest in the curve.

The investigation on abolishing the rhythm brought to light several facts: (1) The muscular activity and metabolic rhythms are parallel. (2) Continuous lighting alone for a month did not abolish the diurnal rhythm. (3) Continuous feeding alone (feeding $\frac{1}{8}$ of the day's maintenance ration every 3

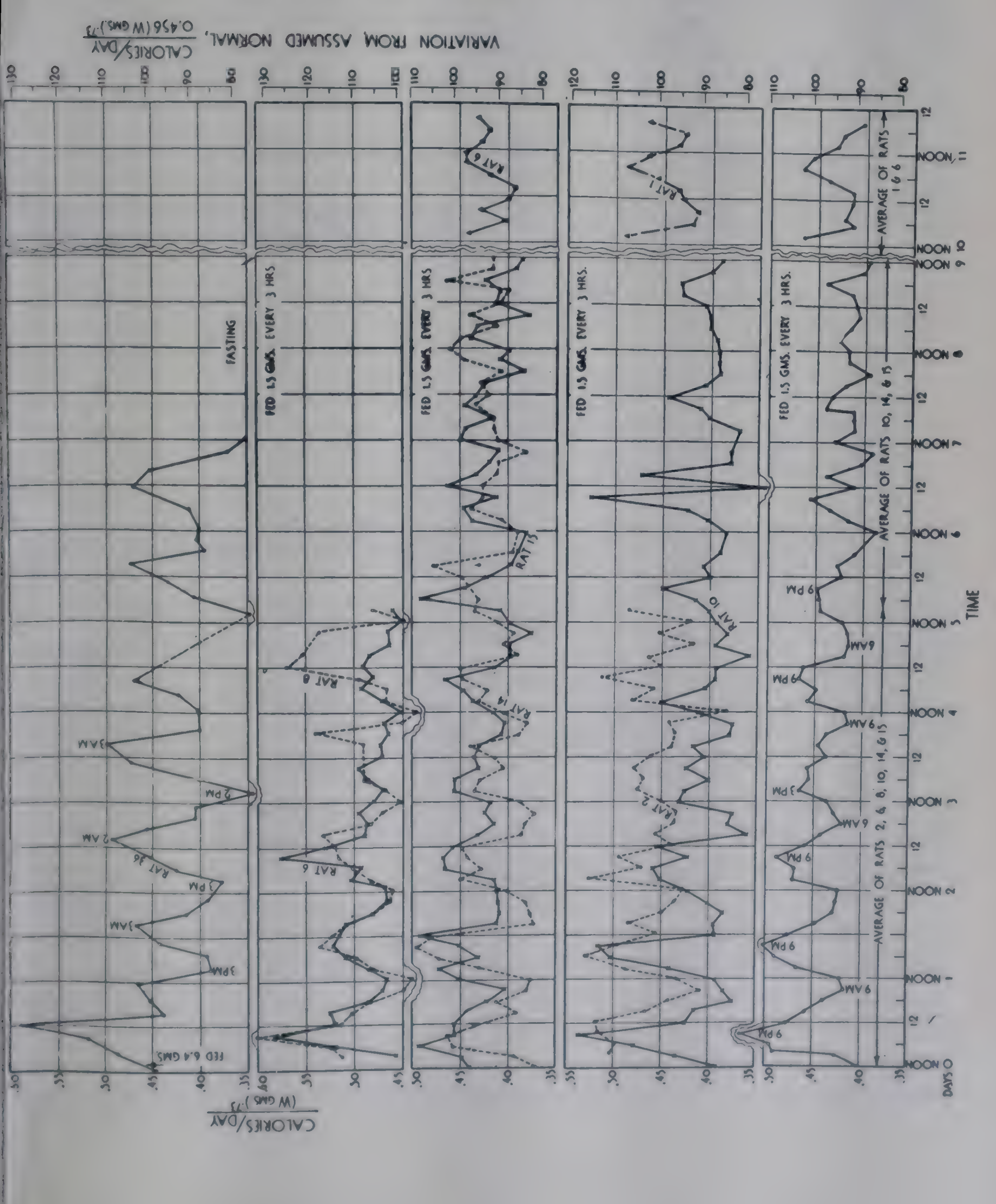

Fig. 9.3. Diurnal metabolic rhythms of white rats under continuous light of constant intensity when fasting (upper curve), and when consuming $\frac{1}{8}$ of the maintenance ration at 3-hour intervals throughout day and night for over a week (lower curves). The rhythm is maintained in the fasting rat, but is extinguished in the continuous-feeding rats, so that only residual "autogenous" rhythms remain.

hours) for a month did not abolish the rhythm. (4) A week of fast under continuous lighting did not abolish the rhythm. (5) But a combination of continuous lighting and continuous feeding ($\frac{1}{8}$ of the daily ration every 3 hours) extinguished both the activity and the metabolic rhythms.

The metabolic result of fast under continuous lighting is shown in the top curve of Fig. 9.3. The first midnight peak is above the other peaks because it includes the heat increment of feeding (*SDA*) of the prefasting meal (6.4 g feed eaten at 3 p.m.); it includes, in other words, (1) the *normal* 25 per cent diurnal metabolic difference and (2) a 25 per cent feed intake effect. This is shown by the following data:

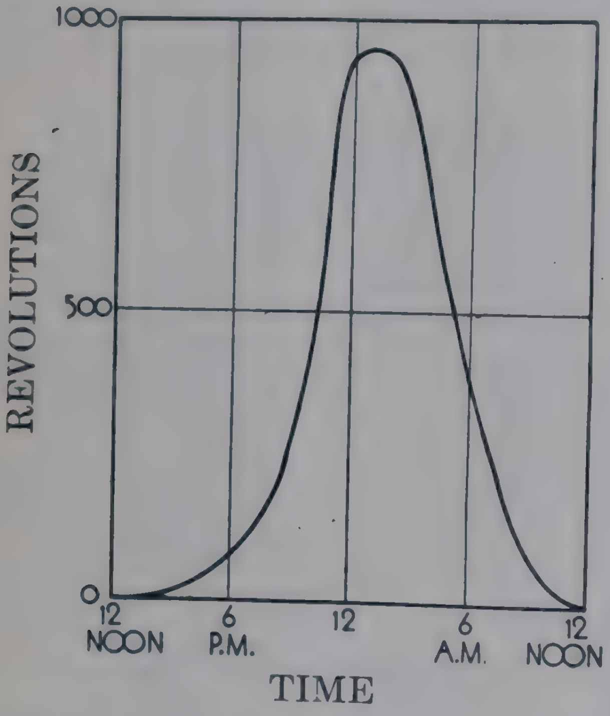

Fig. 9.4. Diurnal activity in the rat measured by the revolution in an exercise drum.

24-hour period of fast	Metabolism: Maximum Cal/day	Maximum time	Minimum Cal/day	Minimum time	Difference (%)
1	37.4	midnight	24.4	3 p.m.	53.3
2	30.7	9 p.m.	23.2	3 p.m.	52.3
3	30.2	midnight	24.1	3 p.m.	25.3
4	30.2	3 a.m.	24.0	noon	25.8

In one trial, one group of rats was fed a 10-gram meal at 4 a.m. which was followed not by a rise but a decline in metabolism until noon (8 hours); another group of rats was fed a 10-gram meal at 4 p.m. which was followed by a steady increase in metabolism, reaching a 40 per cent peak increment in 5 to 7 hours; it then declined to a minimum in 16 hours. It is thus evident that there is an algebraic summation of the effects of feed-intake and diurnal rhythm. If the animal feeds during the ascending slope (after 3 p.m.) of the diurnal rhythm, there is a reinforcement of effect with a resulting abnormally high metabolic peak; if it feeds during the descending slope of the rhythm (after 3 to 5 a.m.), the *SDA* is apparently below normal.

The metabolic results on continuous feeding (feeding 1.5 g food every 3 hours day and night) are shown in the middle and bottom curves in Fig. 9.3. Many metabolic, muscular-activity, and respiratory-quotient curves of individual animals and of their averages confirm[42] those in Figs. 9.3 and 9.4.

> "Welsh[43] argued that most diurnal rhythms are 'inherent', since prolonged periods of either continuous darkness or light do not always abolish the rhythms. The diurnal activity rhythm in the rat[44], among others, was cited as an illustration of 'inherent' rhythm. However, we have clearly demonstrated that the diurnal activity and metabolism rhythm in the rat can be quickly abolished under continuous light, provided that this is combined with continuous feeding; and that the rhythm in the young is developed by "social conditioning". The interesting observation is cited[44] that certain phases in the estrous cycle occur at certain definite times in the diurnal rhythm (maximum estrus in the rat occurs at midnight)."

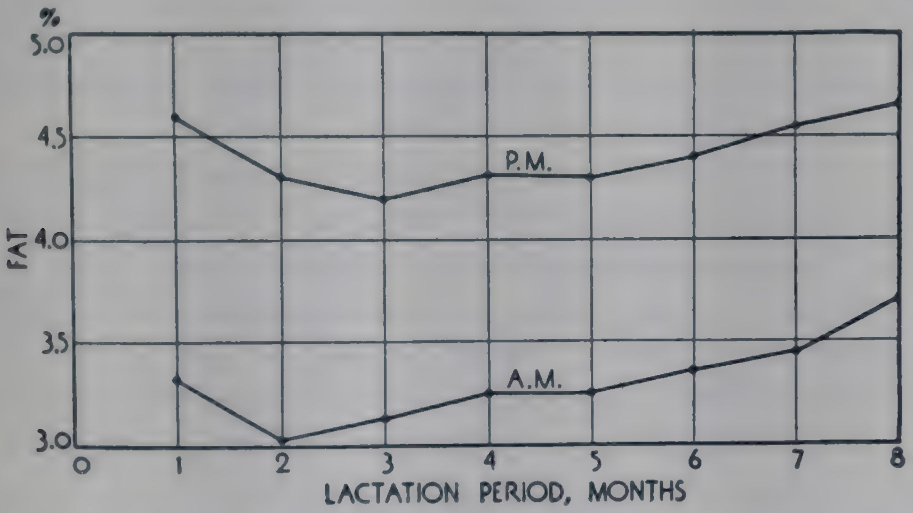

Fig. 9.5. Apparent diurnal rhythm in fat percentage in morning (a.m.) and evening (p.m.) milk during the lactation period.

9.4: Summary. There is an impressive analogy between diurnal rhythms discussed in this chapter and seasonal rhythms discussed in the preceding chapter, both being ultimately actuated by the sun-earth rhythm; metabolic effects, however different in nature, are exerted not only on plants endowed with chlorophyll but also on animals endowed with eyes. The timing of the rhythmic activity in animals depends on the nature of their visual apparatus, whether they are adopted for relatively dim night light or bright daylight.

The diurnal difference between the metabolic peak and trough is shown to be about 25 per cent of the average. The metabolic rhythm reflects activity, feeding, nervous irritability, and related rhythms, although the metabolism was measured during rest.

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[42] Detailed curves of the rhythms of muscular activity, respiratory quotients, metabolism, and also descriptions of apparatus are given in the original report, Univ. Missouri Agr. Exp. Sta. Res. Bull. 274.

[43] Welsh, J. H., "Diurnal rhythms," *Quart. Rev. Biol.*, **13,** 123 (1938). Browman, L. G., "Light in its relation to activity and estrous rhythms in the albino rat," *Anat. Rec.*, **67,** Suppl. 1, p. 107 (1936). Werthessen, N. T., "A study of the variation in the metabolic rate of man and rat," *Anat. Rec.*, **67,** Suppl. 1, p. 43 (1936). "The significance of subnormal respiratory quotient values induced by controlled feeding in the rat," *Am. J. Physiol.*, **120,** 458 (1937).

[44] Hemmingsen, A. M., and Krarup, N. B., "Rhythmic diurnal variation in the estrus phenomena of the rat and their susceptibility to light and dark." Det Kgl. Danske *Videnskabernes Selskab. Biolgiske Meddelelser*, **13,** #7 (1937) 61 pp. (Article in English.)

These rhythms in adults have their ultimate developmental roots in the sun rhythm, transmitted and amplified in the organism by the nature of the visual apparatus, and secondarily in a superimposed social conditioning. The nocturnal rat, for example, develops ingrained habits—conditioned reflexes—of sleeping during the day and feeding, etc., during the night. These reflexes gradually come to include muscle tone, urination, defecation, and intermediate metabolism, including blood composition and perhaps body composition. These rhythms are so persistent that in the rat they cannot be extinguished by a month of continuous light alone, nor by a month of continuous feeding (at 3-hour intervals $\frac{1}{8}$ of the day's maintenance ration) alone, nor by a week of continuous lighting and fasting. But a combination of continuous lighting and continuous feeding ($\frac{1}{8}$ of daily ration every 3 hours) extinguished the metabolic rhythm in about a week.

In addition to their scientific and philosophic interest (from the organismic viewpoint) these rhythms are practically important in studies on the influence of desired conditions on metabolism and related phenomena. Unless the rhythm is taken into consideration, or is extinguished as described in the text, the metabolic (or related activity) difference due to the conditioned diurnal and related rhythms may exceed the metabolic differences caused by the factors under investigation and thus confuse the problem.

In addition to the diurnal rhythms, there are shorter rhythms in the rat, such as Richter's two to four-hour 'spontaneous' rhythms, 3-hour feeding and 'washing-up' rhythms, and numerous digestive, circulatory, respiratory, secretory and excretory rhythms, blood and tissue (especially liver and adrenal) composition, and brain-potential rhythms, all of which influence the metabolic level. There are also longer rhythms. Activities of rats in revolving cages[45] indicate the presence of 4-day rhythms, and even longer sex- and seasonal-cycle rhythms. There are also several longer body-temperature rhythms in humans. Thus Zucker[46], Cary[47], and many others, reported monthly body-temperature rhythms in women, the lowest temperature coinciding with ovulation and increased cervical secretion (Ch. 7).

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[45] Cf., Wang, G. H., "Spontaneous activity and the estrous cycle in the white rat," Comp. Psychol. Monographs, 2, 1 (1923); Slonaker, J. R., "The normal activity of the white rat at different ages," J. Comp. Neurol. Psychol., 17, 342 (1907). Slonaker, J. R., "The effect of pubescence, castration, and the menopause on the voluntary activity of the albino rat," Am. J. Physiol., 68, 294 (1924). Richter, 1927; Sherwood, T. C., "The relation of season, sex, and weight to the basal metabolism of the albino rat," J. Nutr., 13, 223 (1936); Smith, A. H., and Anderson, J. E., "The effect of quantitative and qualitative stunting on maze learning," J. Comp. Psych., 6, 337 (1926); "Relation of performance to age and nutritive condition in the white rat," Id., 13, 409 (1932); and so on.

[46] Zucker, T. F., J. Obst. and Gynec., 36, 998 (1938).

[47] Cary, W. H., J. Am. Med. Assn., 114, 2183 (1940).

Chapter 10

Homeostasis and Organismic Theory

In a world struggling for unity, borderlines between the different spheres of human thought become unessential. *Thomas Mann*

Vital mechanisms have one object, preserving constant the internal environment. *Claude Bernard*

About the year 1857 Johannes Müller broke down mentally trying to keep abreast of the literature on physiology. *E. J. K. Menge*

10.1: Introduction. This, like Chapters 1 and 25, is an integrating chapter. It discusses a general principle in biology, analogous to the principle of Le Chatelier[1] or the principle of least action in physical science, or to the principle of sufficient reason in philosophy. We must have binding concepts to give us the feeling of orderliness and keep us from developing a Johannes Müller neurosis. The principle is, in brief, that all organisms and also societies of organisms[59]—epiorganisms (Gerard) or supraorganisms (Emerson)—react to changing conditions in such manner as to maintain constant what Claude Bernard[2] designated as their "internal environment".

While the body's powers of adjustment to different conditions have been long known, this knowledge had not become a central principle of physiology—and now of sociology[59]—until Claude Bernard's dramatic formulation, supported by the penetrating contributions of Haldane[3], Loeb[4], Henderson[5], Cannon[6], Barcroft[7], and many others[8].

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[1] Le Chatelier, H., "Récherches expérimentales et théoretiques sur les equilibres chimiques," Paris, 1888.

[2] Bernard, C., "Leçons sur les phenomenes de la vie," Paris, 1878 (see especially pp. 113-121). See also "Introduction to the study of experimental medicine," 1926 (based on "Leçons de physiologie expérimentale appliquée à la médecine," Paris, 1855, and "Introd. à l'étude de la Médecine expérimentale," Paris, 1885).

[3] Haldane, J. S., "Respiration," New Haven, 1922, and many other books and journal articles. For the often mystic flavor of his interpretations, see his, "Philosophical Basis of Biology," London, 1931; also, "Mechanism, life and personality," New York, 1914; "The sciences and philosophy," New York, 1929; "The Philosophy of a biologist," Oxford, 1935.

[4] Loeb, J., "The organism as a whole," New York, 1916; also "The mechanistic conception of life," Chicago, 1912, and "Forced movements, tropisms, and animal conduct," Philadelphia, 1918.

[5] Henderson, L. J., "The fitness of the environment", New York, 1913; "Blood, a study in general physiology," New Haven, 1928, "The excretion of acid in health and disease," Harvey Lectures, 1914-15, pp. 132-53; "Physiologic regulation of the acid-base balance of the blood and some related functions," *Physiol. Rev.*, **5**, 131 (1925). In addition to the above books and reviews, the following papers by Henderson on control of

One of Bernard's generalizations is that the degree of an organism's independence of its environment is proportional to its ability to maintain constant its internal environment: *la fixité du milieu intérieur est la condition de la vie libre*; and that the organism is a closely knit community, the component members of which are organized to keep the internal environment constant in the face of fluctuating external conditions (examples of "physiologic constants": blood pH, body temperature, blood pressure, pulse rate, etc.).

We shall employ Cannon's designation[6] *homeostasis* to describe this principle, this tendency to maintain a "steady state" (*homeo* from the Greek, like or similar; *homoio*, the same).

Homeostasis, the integrated cooperation of all the organs and systems in the body—nervous, endocrine, circulatory, excretory, digestive, and so on—in the maintenance of a "steady state" equilibrium may be considered as one aspect of what is often referred to as organicism[9], holism[10], gestalt[11], and related concepts including, on other planes, perhaps dialectic materialism[12], multiple causation, and so on[13].

While some phases of adaptation of organism or supraorganism may be considered as special cases of the theorem of Le Chatelier, formulated for non-living systems, homeostasis is reserved for biologic (and sociologic in this book) changes which do not necessarily occur in the same direction, as they would in a non-living system. Thus changing environmental temperature does not necessarily change body temperature but sets in motion thermo-

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acidity are classics: "Equilibrium in solution of phosphates," *Am. J. Physiol.*, **15**, 257 (1906); "Neutrality equilibrium in blood and protoplasm," *J. Biol. Chem.*, **7**, 29 (1909); "A critical study of the process of acid excretion," *J. Biol. Chem.*, **9**, 403 (1911); *Ergeb. d. Physiol.*, **8**, 254 (1909).

[6] Cannon, W. B., "Organization and physiological homeostasis," *Physiol. Rev.*, **9**, 397 (1929); "Aging of homeostatic mechanisms," in "Problems of Aging," Baltimore, 1939; "The wisdom of the body", New York, 1932, 1939.

[7] Barcroft, J., "The brain and its environment," New Haven, 1938; "Features in the Architecture of Physiological Functions", Cambridge University Press, 1934; "La fixité du milieu intérieur est la condition de la vie libre," *Biol. Rev.*, **7**, 24 (1932).

[8] The following books, among others, appeared after this was written: Redfield, R., Ed., "Levels of integration in biological and social systems," Cattell Press, 1942; see especially the essays by R. W. Gerard and A. E. Emerson. Adolph, E. F., "Physiological regulations," Cattel Press, 1943. Gellhorn, E., "Autonomic regulations," Interscience, 1943. Crile, George, "Intelligence, power, and personality," McGraw-Hill Book Co., 1941.

[9] Pike, F. H., *Science*, **76**, 384 (1932). Woodger, J. H., *Quart. Rev. Biol.*, **6**, (1931); *Proc. Aristotelian Soc.*, **32**, 117 (1932).

[10] Smuts, J. C., "Holism and evolution," New York, 1926; *Science*, **74**, 297 (1931).

[11] *Cf.* Koffka, K., "Gestalt psychology." New York, 1935. Koehler, M., "Gestalt psychology," New York, 1929. Lewin, K., "A dynamic theory of personality," New York, 1936. Gestalt is a constellation (or multiple) response to a constellation (or multiple) of stimuli or causative factors.

[12] Needham, J., "Order and life," New Haven, 1936, pp. 44–48. Prenant, M., "La conception matérialiste dialectique en biologie", *Bull. Soc. Philomath.*, **116**, 84 (1933). Needham, J., "Integrative levels," Cambridge, 1941.

[13] Additional references: Sherrington, C. S., "Man and his nature", Macmillan, 1941. Cannon, W. B., *Science*, **93**, 1 (1941). Gerard, R. W., *Sci. Monthly*, **50**, 340, 403, 530 (1940); *Philosophy of Science*, **9**, 92 (1942). Huxley, J. S., *Id.*, **50**, 5 (1940). Jennings, H. S., *Science*, **92**, 539 (1940). Fulton, J. F., "Physiology of the nervous system," 1938.

regulatory apparatus to counteract the external change (Ch. 11). Administration of thyroxine to normal individuals does not necessarily increase the metabolic rate, but sets in motion mechanisms for suppression of the body's own thyroxine production (Ch. 7). Reducing oxygen pressure in the air (by climbing a mountain, or in a low-pressure chamber) does not necessarily reduce the oxygen supply to the cells but sets in motion regulatory changes (such as increasing the hemoglobin concentration in blood and other oxygen-carrying mechanisms and—the latest observation—probably increases the concentration of the oxidation catalysts in the body as indicated, for example, by increased excretion—and therefore production—of ascorbic acid in rats on placing them in a low-pressure chamber). Biologic reactions are, evidently, not always explicable on the customary physical or chemical levels (Ch. 16) but on unique *organizational* levels which may not be present in non-living systems. This appears to be recognized as indicated by the following remarks: life is not a characteristic of atoms, molecules, or genes as such, but of a certain organization of the parts of the living organism (E. G. Conklin); the laws of physiology are laws of *organization* (Claude Bernard); physiology is concerned with *sociological* laws, laws of *organization and adaptation* (A. Carrel); the unique problem of physiology is to discover the *relatedness* to one another of the details of structure and function (J. S. Haldane). Darwin has said that evolution is change in form in successive generations *in response* to certain influential factors in the environment.

The concept of homeostasis, especially if it is extended to include societies of organisms as well as individuals, has very far-reaching implications. Indeed, every one of the preceding and following chapters is an illustration of the effectiveness of homeostasis. Thus the following chapter is concerned with homeothermy, the homeostatis of body temperature. Chapter 24 deals with homeostasis in muscular work, that is, the maintenance of a constant level of oxygen and carbon dioxide in the blood in the face of greatly increased oxygen consumption and carbon dioxide production during heavy muscular exercise. Chapters 13 to 15 discuss the homeostasis of metabolism in relation to surface area and to change in form. Chapter 17 is concerned with homeostasis in relation to the ratio of surface area and of strength of the supporting structures to increase in body weight. Chapter 16 deals with the homeostasis of growth: growth proceeds as if the "normal" condition were that represented by the mature size, and the rate of growth tends to be proportional to the distance from the mature size. Chapter 18, on senescence, is concerned with failing homeostasis; and so on, as illustrated by some of the following sections which could be expanded indefinitely.

Pathology may be considered as the study of attempts to maintain homeostasis under conditions of injury. When injury occurs, processes are set in motion to correct it. The tendency to wound healing is, indeed, so great that we pay little attention to it. Even a heart afflicted with coronary sclerosis

(Ch. 18) may function for many years by various compensations, even to the extent of establishing new collateral circulatory vessels to take over the functions of the sclerotic ones. Reproduction of the organism as a whole, as of its constituent cells, may be considered as a compensatory, or homeostatic, mechanism against senescence, maintaining constant the internal social environment in spite of the aging of its constituent members.

The study of homeostasis is, then, the analysis of factors that maintain an advantageous dynamic steady state in biologic systems in the face of conditions that oppose it.

Let us discuss a few illustrative homeostatic mechanisms in detail. In the interest of simplicity each of the following sections is devoted to a different homeostatic mechanism. These mechanisms do not, however, necessarily function independently.

10.2: Body-weight regulation[14]. Some readers may recall that their body weight had not changed as much as five pounds over many years, in spite of widely differing conditions of life. Some may also recall the difficulties encountered in attempting to increase or to decrease body weight. The body appears to have automatic regulatory, or homeostatic, mechanisms stronger than purposive resolves to change body weight. Two or three of these mechanisms have been investigated.

One, the decline in digestibility, metabolizability, and assimilability (or increased losses in feces, urine, and heat increment of feeding, or *SDA*) has been discussed (Ch. 5). The more food consumed, the less the nutritive utilization per unit food; conversely, the less food consumed (within certain limits), the higher the utilization per unit food.

Then, too, the higher the food intake, the higher the body weight and, therefore, the greater the proportion of the food that goes to maintain the body; conversely, the lower the food intake and the lower the body weight, the less it costs to maintain the body. In brief, the dietary maintenance tax is adjusted to the dietary input; when placed on a reducing diet the organism becomes more economical, thus counteracting weight reduction; on an abundant diet, the organism becomes more and more extravagant, counteracting undue fattening. The body persists in maintaining its "normal" weight.

Our colleague Addison Gulick[15], characterized by a spare or non-fattening type of "normality", reported in a dramatic manner his strenuous but relatively unsuccessful attempts to gain weight. Gulick "explained" his unsuccessful attempts to gain weight by referring to "spendthrift oxidation during overnourishment" and "economical oxidation during undernourishment".

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[14] For a recent discussion of the physiologic mechanisms adjusting intake to output, or gains to losses, of body weight, including water, energy, and nitrogen, see Gasnier, A., and Mayer, A., *Ann. Physiol. Physicochim. biol.*, **15**, 145, (1939) (nature and number of regulatory mechanisms); p. 157 (nutritional regulatory mechanisms in the rabbit); p. 186 (regulatory mechanisms of metabolic intensity); p. 195 (breed differences in rabbits); p. 210 (individual differences).

[15] Gulick, A., *Am. J. Physiol.*, **60**, 371 (1922).

Anderson and Lusk[16] investigated the efficiency of a dog working under various conditions of food supply. The dog showed greater energy expense when in an overnourished than in a spare condition. Zuntz and Loewy[17] reported 10 and 16 per cent reductions in their basal energy metabolism when placed on the spare German war diet. Benedict[18] and associates reported 20 per cent reduction in basal energy metabolism in young men on a reduced diet involving a loss of 130 g nitrogen.

All in all, the body has very effective automatic mechanisms to prevent interference by purposive meddlers with its normal, that is, its hereditary, weight.

The homeostatic regulation of body weight is evidently of great agricultural importance. High feeding accelerates the fattening process, but it occurs at a greatly increased energy cost; conversely, the leaner the animal at the beginning of a fattening trial the more economic its gains. In general, the economy of gain tends to be proportional to the distance from the "finished condition" (Chs. 5 and 22).

Though we are not here concerned with detailed causal mechanisms, it may be noted that the immediate hunger mechanism was shown by Cannon[19] and by Carlson[20] to consist of contractions of the stomach walls. The contraction *hunger* pain is reinforced by *appetite*, psychic longing for the remembered sensation of feeding.

Bulato and Carlson[21] reported that hunger contractions may be produced at will by reducing the blood sugar by insulin injection, indicating that reduction of blood sugar produces the stomach contractions. There is no doubt that food consumption and weight gains are greatly increased by administration of insulin in proper form (protamine zinc insulin)[22]. However, it has not been proved that the normal hunger sensations are caused by lowering the blood-sugar level. But whatever the mechanism, it is effective in maintaining the body at its hereditary weight level.

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[16] Anderson, R. J., and Lusk, G., *J. Biol. Chem.*, **32**, 421 (1917).

[17] Zuntz, N., and Loewy, A., *Berl. Klin. Wochsch.*, 825 (1916); *Biochem. Z.*, **190**, 244 (1918).

[18] Benedict, F. G., Miles, W. R., Roth, P., and Smith, H. M., Carnegie Inst. Pub. 280, 1919.

[19] Cannon, W. B., "Digestion and health," New York, 1936; Cannon and Washburn, A. L., *Am. J. Physiol.*, **29**, 441 (1912).

[20] Carlson, A. J., "The control of hunger in health and disease," Chicago, 1916.

[21] Bulato, E., and Carlson, A. J., *Am. J. Physiol.*, **69**, 107 (1924).

[22] MacKay, E. A., Callaway, J. W., and Barnes, R. H., "Hyperalimentation in normal animals produced by protamine insulin", *J. Nut.*, **20**, 59 (1940). Long, M. L., and Bischoff, F., "Effect of insulin upon body weight of rabbit," *J. Nut.*, **2**, 245 (1930). Maclagan, N. F., "Role of appetite in control of body weight," *J. Physiol.*, **90**, 385 (1937). Macleod, J. J. R., Magee, H. E., and Middleton, W., "Insulin and increase in weight of young animals," *Bioc. J.* **24**, 615 (1930).

10.3: Body-water regulation[23]. The fat-free body of cattle contains about 70 per cent water in adults, 90 per cent in the early prenatal period of growth. If the fat is included, the water percentage tends to vary inversely with the fat content, since muscle contains 75 per cent water, whereas the fat depots contain only 6 to 20 per cent. The early embryo, which has little fat, contains[24] up to perhaps 90 per cent water, while the very fat mature steer may contain[24] but 40 per cent water. The various constituents differ in their water content: 99.5 per cent in saliva; 99 per cent in cerebrospinal fluid; 85 per cent in brain gray matter, 68 per cent in brain white matter; 79 per cent in blood; 75 per cent in muscle; 72 per cent in skin; 60 per cent in bone.

Water is being continuously lost through kidneys, alimentary tract, exhaled air and skin. These losses are made good by the automatic thirst mechanism, just as losses in body weight are made good by the hunger mechanism.

When excess water is ingested, the body keeps this water from diluting its internal environment by excretion and by storing it in the muscles and skin which constitute water reservoirs. Thus Haldane and Priestly[25] reported that of 5 liters water taken between 10:45 and 1:15 p.m., 3.2 liters were excreted in the urine by 3 p.m. Apparently none of the remaining water in the body (equivalent to 40 per cent of the blood volume) was found in the blood. There is considerable evidence that the muscle and skin store the excess water temporarily.

Adolph[8] reported that the rate of water excretion is proportional to its excess above the normal level and the rate of water intake is proportional to its deficit below the normal water level.

10.4: Carbohydrate-level regulation[26]. Man does not tolerate a decline in blood-sugar level below about 80 or 70 mg per cent, and if it rises above 160 mg per cent the blood sugar spills over into the urine. The blood sugar in post-absorptive condition is normally 90 to 100 mg per cent, and after a meal about 130 mg per cent. How does the body regulate the blood-sugar concentration within these narrow limits, considering the large quantities of sugar thrown into the blood after a substantial meal, oxidized during heavy muscular exercise, or tapped off during milk production?

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[23] Peters, J. P., "Body water. The exchange of fluids in the body," Thomas, 1935. Harvey lectures, 1937-8. Rowntree, *Physiol. Rev.*, **2**, 116 (1922); Adolph, E. F., *Id.*, **13**, 336 (1933); Adolph, 1943. 8. Darrow, D. C., "Dehydration, acidosis and alkalosis," *J. Am. Med. Assn.*, **114**, 655 (1940). Cannon, W. B., "The physiological basis of thirst," *Proc. Roy. Soc.*, **90B**, 283, (1918); Gregersen, M. I., and Cannon, *Am. J. Physiol.*, **102**, 336 (1932); "Conditions affecting the daily water intake of dogs as registered continuously by a potometer," *Id.*, p. 344. Cannon, "Digestion and health," New York, 1936. See also, Richter, C. P., "Factors determining voluntary ingestion of water," *Am. J. Physiol.*, **122**, 668 (1938).

[24] Univ. Missouri Agr. Exp. Sta. Res., Bulls., 28, 30, 38, 55. For a review see Moulton, C. R., "Age and chemical development of mammals," *J. Biol. Chem.*, **57**, 79 (1923).

[25] Haldane, J. S., and Priestly, J. G., *J. Physiol.*, **50**, 296 (1916). Barcroft[7], 1934.

[26] For review of the literature on the hormonal control of a carbohydrate metabolism see, Russell, J. A., *Physiol. Rev.*, **18**, 1 (1938); Himwich, H. E., *Ann. Rev. Biochem.*, **7**, 143 (1938). Evans, H. M., *Ann. Rev. Physiol.*, **1**, 628 (1938); also the current *Annual Reviews*.

Claude Bernard's researches on the blood-sugar level led to his generalization at the head of this chapter. Bernard's conclusion, amply substantiated, is that the excess glucose is converted into insoluble glycogen and fat. The liver is the major glycogen-storing organ, accounting for from one-fourth to over one-half the total body glycogen; the remainder is distributed in the muscles. The glycogen is reconverted to glucose and fed back to the blood at a rate required to maintain the blood-glucose constant. Insulin (from the islets of Langerhans of the pancreas) is the major hormone involved in this conversion. The blood-sugar level is also regulated by the pituitary (glycotropic hormone), thyroid, and kidney. In addition, the nervous system is involved, by serving as medium of transmission and communication for the bodily needs. The sympathoadrenal system is involved in sugar mobilization in emergencies (see Cannon[49]).

While excess sugar in the blood does not produce important subjective symptoms, blood-sugar deficiency leads to feelings ranging from hunger through nervousness and weakness, to convulsions following an excessive dose of insulin injection (insulin or hypoglycemic reactions). Objective symptoms are pallor, rapid pulse, dilated pupils, profuse sweating, and convulsions. The brain obtains its energy perhaps exclusively from sugar[27, 28]. For this reason, in part, sugar deficiency in blood, for example, insulin hypoglycemia, leads to serious nervous disturbances[29] (Sect. 20.2).

Blood-sugar regulation declines with age following 30 or 40 years[30], perhaps because of defective glycogen storage in the liver[31].

10.5: Calcium-level regulation The parathyroid hormone (parathormone) is the principal regulator of calcium-metabolism[32] (Ch. 7), analogous to insulin, the principal carbohydrate-metabolism regulator. The percentage range of the calcium level in blood (9 to 12 mg per cent plasma) is of the same order as the percentage range of glucose in the blood (80 to 130 mg per cent). There is the additional limitation that the product of calcium and phosphate ions should be constant (in serum the product of Ca and of P in mg is about 36 and the Ca/P ratio between 1 and 2). In other words, the proper functioning of calcium metabolism is also dependent on a certain phosphate[33] concentration, and it might be added, on a certain concentration of parathyroid hormones, vitamin D, and phosphatase enzyme.

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[27] Himwich, H. E., and Nahum, L. H., *Am. J. Physiol.*, **101**, 446 (1932).

[28] Himwich, H. E., *et al.*, *J. Nerv. and Ment. Dis.*, **89**, 273 (1939). Holmes, E., *Biochem. J.*, **24**, 914 (1930).

[29] Himwich, *et al.*, *Am. J. Psychiat.*, **96**, 371 (1939).

[30] Porter, E., and Langley, G. J., "Studies in Blood Sugar," *Lancet*, **2**, 947 (1926). Sellei, C., and Spiera, M., *Biochem. Z.*, **296**, 83 (1938).

[31] Marshall, F. W., "Sugar content of the blood in elderly people," *Quart. J. Med.*, **24**, 257 (1931).

[32] Stewart, C. P., and Percival, G. H., "Calcium metabolism," *Physiol. Rev.*, **8**, 283, and 302 (1928). Shelling, D. H., "The parathyroid in health and disease," Mosby, 1935. Schmidt, C. L. A., and Greenberg, D., *Physiol. Rev.*, **15**, 297 (1935). Aub. J., *J. Am. Med. Assn.*, **109**, 1276 (1937); see Ch. 7.

[33] Rickets is often the result of phosphorus deficiency, as also of calcium deficiency.

The equilibrium between calcium ion on one hand and insoluble bone [$CaCO_3 \cdot 2$ to $3Ca_3(PO_4)_2$] on the other, is analogous to the equilibrium between blood sugar and glycogen.

Just as hypoglycemia affects the nervous system (mostly the cortical function), so hypocalcemia affects the nervous system (mostly the autonomic and peripheral nervous systems). Milk fever (in dairy cattle) is a familiar agricultural example of hypocalcemia.

10.6: Fat-level regulation[34]. The blood contains lipoids in the form of total fatty acids or "total lipid" 300 to 500 mg per cent; cholesterol esters 150 to 190 mg per cent; lipid phosphorus (lecithin) 12 to 14 mg per cent; or phospholipid about 140 mg per cent (in plasma) to 420 mg (in corpuscles). However, very much higher values were recorded in essential hyperlipemia[35]. Ingestion of a meal of fat results in "alimentary lipemia", associated with a rise of fat in blood to 2 or 3 per cent.

As sugar or calcium concentration remain nearly constant by storing or drawing on glycogen or bone, so the lipoids remain roughly constant by storing fat in various fat depots when there is excess of it, and drawing on these fat depots when there is scarcity of food.

The physiologic control of lipoid transport has been investigated most extensively by Bloor[34]. As a calcium hexose monophosphate is the important intermediary in calcium metabolism and calcium homeostasy, so lecithin, also a phosphorus-containing substance[36], appears to be the important intermediary in lipoid homeostasy. It was noted (pp. 128 and 133) that lecithin (or choline) deficiency leads to the formation of fatty livers and "cholesterol livers"[37].

10.7: Oxygen and acid level regulation. The process of living involves the consumption of enormous quantities of oxygen and production of equivalent quantities of acids (carbonic, sulfuric, phosphoric, etc.). Yet both oxygen and acid levels deviate insignificantly from the "normal" level even during

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[34] Bloor, W. R., *Physiol. Rev.*, **2**, 107 (1922); *Chem. Rev.*, **2**, 243 (1925); "Harvey Lectures", p. 39, 1923–24, and more recent reviews in *Ann. Rev. Biochem*; "Biochemistry of Fatty Acids," Reinhold, 1943.

[35] Bernstein, S. S., *et al.*, "A child with essential hyperlipemia," *J. Pediatrics*, **14**, 570 (1939), cited the following data, mg 100 cc blood.

	Total lipids		Phospholipids		Neutral fat		Free cholesterol		Cholesterol esters	
	Plasma	Erythrocytes	Plasma	Corpuscles	Plasma	Corpuscles	Plasma	Corpuscles	Plasma	Corpuscles
Normal 6-yr old	452	418	140	240	94	44	33	99	184	34
The hyperlipimid child	3100 4200	650–760	440–520	480	2100–3200	50–450	130–200	80–95	430–700	80 95

[36] For the formula of lecithin, see page 128.

[37] Best, C. H., and Ridout, J. H., *Ann. Rev. Biochem.*, **8**, 349 (1939).

muscular exercise, when the oxygen consumption and carbonic acid production may increase ten-fold (Ch. 24). This constancy of internal environment is brought about by several mechanisms, from increased ventilation rate and circulation rate (Ch. 24) to increased hemoglobin concentration. Thus ascending Mount Everest about 20,000 feet, where the oxygen pressure is 50 per cent of that at sea level, the blood hemoglobin may increase from 4 million cells/cc to over 8 million. Moreover, a hemoglobin unit in high-mountain dwellers can carry more oxygen, as illustrated by the following data from Dill[38] on high-mountain dwellers.

	Vicuna (high-mountain dweller)	Man	Domestic Sheep
Volume % arterial O_2	18.0	14.4	8.4
Volume % venous O_2	4.0	2.4	1.0
Difference	14.0	12.0	7.4

Then, too, under sudden demand for oxygen the blood stored in the spleen and liver is released to help with the oxygen transport. Barcroft[39] reported that the spleen of a dog was reduced to ¼ normal size when the dog was set to chase a cat. Scheunert and Krzywanek[40] reported increased blood counts in horses during exercise. Rein[41] reported that the liver released 25 per cent of its blood under the influence of adrenaline. In brief, exercise and other conditions which involve increased oxygen use are associated with increased hemoglobin concentration.

It is interesting to recall that in the later stages of gestation fetal growth proceeds at an increasingly relative faster rate than the placenta, resulting in decreased oxygen supply to the fetus. The blood picture of the new-born shows the effects. This prompted the remark (by Barcroft?) that during the last stages of gestation the embryo lives in a Mount Everest atmosphere and is acclimated to it. For this reason, in part, new-born and very young animals have very high hemoglobin concentration and, in general, tolerate anoxia very much better than older ones (Ch. 14).

The exceptional ability of whales, seals, and beavers to remain submerged for half an hour depends (Ch. 24) on these homeostatic reserves: large blood volume, high hemoglobin concentration, the ability to go into great oxygen debt, and especially the ability to shunt the blood (which carries the oxygen) to the central nervous system (most sensitive to oxygen want) from the other tissues, those less sensitive to oxygen want. Anoxia is also associated with lowered body temperature and, therefore, reduced metabolism and depressed oxygen need.

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[38] Dill, D. B., "Life, heat, and altitude," Cambridge, Mass., 1938. Altitudes and air pressures: Mount Everest having an altitude of about 29,000 feet, has an air pressure which is about 35 per cent of sea level pressure; Pikes Peak, 13,000 feet high, about 60 per cent sea level pressure; Mexico City or Santa Fé about 8,000 feet, about 78 per cent sea-level pressure; Denver, about 5,000 feet, about 83 per cent sea-level pressure. Hall, F. G., Dill, D. B., and Barron, E. S. G., *J. Cellular and Comp. Physiol.*, **8**, 301 (1936).

[39] Barcroft, J.,[7], also *J. Physiol.*, **68**, 375 (1930). Izquierdo, J. J., and Cannon, W. B., *Am. J. Physiol.*, **84**, 545 (1928). (Fear and rage increase red blood count.)

[40] Scheunert, A., and Krzywanek, F. W., *Pfluger's Arch.*, **213**, 198 (1926).

[41] Grab, W., Janssen, S., and Rein, H., *Klin. Woch.*, **33**, 1539 (1931).

Since lack of oxygen and lack of glucose have the same end effect on brain metabolism, the nervous symptoms described for hypoglycemia also hold for anoxia[42].

The mechanism of blood-acidity regulation was worked out chiefly by Henderson[43, 5]. The blood pH ranges only[44] from 7.30 to 7.45. Even feeding sulfuric acid (over a liter a day of N H_2SO_4 to hogs[45]) did not change it.

The maintenance of constant pH of the blood is accomplished by (1) preliminary neutralization by the blood buffers (bicarbonates, phosphates, hemoglobin, and also by ammonia), (2) excretion of the volatile acids (CO_2) by the lungs, and (3) excretion of the non-volatile acid by the kidneys.

10.8: Neuro-endocrine homeostasis. We have seen (Ch. 7) that if the metabolic hormone thyroxine is injected, the body "tries" to keep the metabolic level constant by reducing its own production of thyroxine. Similarly, if the sex hormone estrogen is injected, the animal "tries" to maintain its normal sex activity level by reducing the production of its own estrogen. Both of the controls are carried out by way of the pituitary, by depressing the production of thyrotropic and gonadotropic hormones respectively. The same mechanism is employed for many other hormones controlled by the pituitary.

Dairymen know that milking stimulates and cessation of milking depresses milk production. Now milk production is dependent on pituitary lactogenic hormone production, and it appears[46] that suckling stimulates it, obviously by a nervous path. The closely related maternal reflexes are even more intimately dependent on the central nervous system, including the higher brain centers[47].

The dietary control of insulin production is interesting. On heavy feeding, the islets of Langerhans hypertrophy, producing more insulin to take care of the excess sugar. However, this often sets up a vicious cycle: the more food, the greater the hyperinsulinism and the greater the hyperinsulinism the greater the desire for food. This leads to obesity and frequent degeneration of the islets of Langerhans due to overwork[48]. Here we have a type of homeostasis which by its immediate correction leads to ultimate failure.

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[42] Himwich, *et al.*,[29] (1939), Barcroft[39] (1938), Gellhorn[8] (1943). Van Liere, E. J., "Anoxia", Univ. Chicago Press, 1942.

[43] Henderson, L. J., and Palmer, W. W., "Acidity of urine," *J. Biol. Chem.*, **13,** 393 (1912), and **14,** 81 (1914). Henderson, L. J., [5]; also Van Slyke, D. D., *et al.: Physiol. Rev.* **7,** 141 (1921); *J. Biol. Chem.*, **30,** 281 and 401 (1917); **48,** 153 (1921); **52,** 525 (1922); **54,** 481 and 507 (1922); **79,** 769 (1928); Peters and Van Slyke. "Quantitative Clinical Chemistry," 1931, Williams and Wilkins. Barcroft,[7] and Haldane[3].

[44] Dill, D. B., Talbot, J. H., and Edwards, H. T., *J. Physiol.*, **69,** 267 (1930).

[45] Lamb, A. R., and Evvard, J. M., "The effect of organic and mineral acids on growth, reproduction, and metabolism in swine," Iowa Agr. Exp. Sta. Res. Bull., 70, 1921.

[46] See Turner, Ch. 7. Selye, H., *et al.*, *Endocrinology*, **18,** 273 (1934). Reece, R. P., and Turner, C. W., *Proc. Soc. Exp. Biol. Med.*, **35,** 621 (1937).

[47] Leblond, C. P., and Nelson, W. O., *Am. J. Physiol.*, **120,** 167 (1937). Leblond, *J. Gen. Psychol.*, **57,** 327 (1940).

[48] Brody, S., *Ann. Rev. Biochem.*, **4,** 384–6 (1935).

There are other examples of the same type. Thus strong emotions lead to nerve excitation (parasympathetic, vagi, sacral) and production of excessive amounts of acetylcholine, sympathin, histamine, adrenaline, and so on favoring the overcoming of the immediate emergency but often with unfavorable long-range effects (Ch. 18) on the circulatory and digestive systems. Exophthalmic goiter is attributed by Crile (Ch. 18) to overexcitement.

A familiar example of the effect of nervous stimuli on endocrine activity, which has a homeostatic basis, is the mobilization of sugar (hyperglycemia) during emergency to furnish the energy for the forthcoming effort; if the effort does not materialize on a physical plane (as in the case of a spectator at a foot-ball game who does not himself fight although emotionally geared thereto), the sugar is eliminated by the kidney, constituting the well-known emotional glycosuria, thus keeping the blood sugar level constant (Cannon's emergency theory[49], see Sect. 7.3.2B).

Some emotions become habitual, chronic, "structured", or conditioned, such as those investigated by Pavlov[50]. These are of great agricultural as well as social importance. Good animal husbandmen appreciate the importance of gentle treatment of their animals, and are aware of the unpleasant conditioned reflexes, or habits, that may develop, especially in horses and dairy cattle. As Mark Twain has said, habit is habit, not to be flung out of the window by any man.

Rapid salt loss due to any one of many causes, such as adrenalectomy[51], diabetes insipidus[52], or sweating is associated with corresponding craving for salt[53]. On the other hand, extreme salt consumption is often a diagnostic symptom of adrenal and related diseases. Indeed, it has been suggested that taste thresholds may serve as delicate indices of nutritional deficiencies[54].

Parathyroidectomy, which disturbs calcium metabolism, is associated with greater (four-fold) calcium (lactate) intake[55]. In the absence of calcium more magnesium and even strontium salts are consumed. During pregnancy and lactation protein and mineral (but not carbohydrate) intake is increased[56].

Vitamin B is essential for carbohydrate oxidation; hence the aversion for carbohydrate (and protein) and craving for yeast on a vitamin B-deficient diet[56, 57]. However, this homeostatic mechanism does not function precisely.

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[49] Cannon, W. B., *et al.*, *Am. J. Physiol.*, **69**, 46, (1924). Cannon, "The James-Lange theory of emotion," *Am. J. Psychol.*, **39**, 106 (1927). Cannon, "Bodily changes in pain, hunger, fear and rage," New York, 1929, and "The wisdom of the body," 1932.

[50] Pavlov, I. P., "Conditioned reflexes." London, 1927. Deutsch, F., "The production of somatic disease by emotional disturbances", *in* "The inter-relationship of mind and body," Vol. 19, Assn. Res. Nerv. and Mental. Dis. Pub., Baltimore, 1939.

[51] Richter, C. P., and Eckert, J. F., *Endocrinology*, **22**, 214 (1938).

[52] Swann, H. G., *Science*, **90**, 67 (1939).

[53] Richter, C. P., *Endocrinology*, **24**, 367 (1939).

[54] Richter, and MacLeod, A., *Am. J. Physiol.*, **126**, 1 (1939).

[55] Richter, C. P., and Eckert, J. F., *Endocrinology*, **21**, 50 (1937). See also MacCallum, W. G., and Voegtlin, C., *J. Exp. Med.*, **11**, 118 (1909), and *Bull. Johns Hopkins Hosp.*, **19**, 91 (1908).

[56] Richter, *et al.*, *Am. J. Physiol.*, **124**, 596 (1938).

[57] Jukes, C. L., *J. Comp. Psychol.*, **26**, 135 (1938).

Thus chickens do not differentiate between riboflavin-rich and riboflavin-poor diets even if they are riboflavin-starved[57]. Many other examples could be cited[58].

Appetite, then, appears to be in many cases, but not in all, an important guide to "nutritional wisdom" or homeostasis, provided that it is not conditioned adversely in early life. The wide popularity of "sweets" and white bread may be the result of early conditioning by a wrong "psychodietetics". It is interesting to note that such animals as dairy cattle and high-laying fowl raised under relatively artificial systems rather lack nutritional wisdom, and the same is true of children (Sect. 20.5).

10.9: Social homeostasis.[59] A multi-cellular organism may be viewed as a community of individual cells specialized to perform various functions for the community as well as for carrying out their own basic metabolic or life processes. Such a viewpoint suggests an analogy between an *individual* multi-cellular organism, for example an ant, termite, or bee, and a society of organisms, or supraorganism, for example, a *colony* of ants, termites, or bees. The multicellular individual termite is derived from a single egg cell. The cells of the individual differentiate, by virtue of their positions in the body, into the various specialized cells and tissues. Similarly, the colony of termites or bees is derived from virtually a single egg cell, the individuals of which differentiate, by different feeding methods and other conditions, into various specialized individuals—workers, soldiers, drones, queens, and so on.

In some species at some time it is indeed impossible to distinguish between a multicellular individual and a closely integrated group of individuals. Not only are the two categories alike in being composed of the same ultimate substances, carrying on the same metabolic processes, having similar adaptive mechanisms, but both are stages in the evolution of ever larger and more integrated "orgs". It will be shown (Chs. 16 and 19) that the age curves of growth of individuals, such as rats or pumpkins, are so similar to the time curves of growth of populations (of yeast, bacteria, flies, men) that all the curves can be made to coincide.

This analogy between the individual organism and society of organisms extends to social homeostasis, of which social insects (such as termites, ants, bees, and so on) furnish striking examples on one organizational level. But one may cite examples of homeostasis on many different levels and in different categories, indicated by the following illustrations.

The reproductive function attains peak activity when growth approaches its end (Ch. 16), that is, when the individual organism begins to get old. Sexual virility may thus be said, figuratively, to coincide with approaching individual senility (Ch. 18). The lawn grass goes to seed most readily when individual life is threatened and on the decline (as in drought, etc.). Reproduction of the individual may thus be viewed as a phase of social homeostasis. By reproduction the "internal environment" of the social organism is kept constant in spite of the aging and dying of its constituent members. Reproduction is a social homeostatic mechanism.

The reproductive process (Ch. 7) is extremely complex and, needless to say, the individual plant or animal does not foresee the social-preservation, or sociocentric, "purpose" of its reproductive drive, just as it does not foresee the individual-preservation, or individuocentric, "purpose" of its hunger and thirst drives. But the ultimate functional aim appears to be to maintain constant the "internal environment" of the social and individual organisms respectively.

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[58] *Cf.* Jones, H. M., *J. Am. Med. Assn.*, **115**, 274 (1940).

[59] *Cf.* Cannon, W. B., "The body physiologic and the body politic," *Science*, **93**, 1 (1941). Gerard[8], and the other essays in Redfield[8]. Brody, S., "Science and Social Wisdom", *Sc. Monthly*, **59**, 203 1944.

The homeostatic mechanisms appear to evolve to ever finer organizational levels. Thus (Ch. 8) reproduction is adjusted, in the social interest, to function in such seasons of the year as will give the new-born animal the best opportunity for survival.

The development, in the most evolved animals (mammals), of the uterus and of mammary methods of raising the young is another illustration of the increased perfection of social homeostasis with advancing evolution. Instead of dropping the unfertilized eggs in the ocean as a fish does, the highly evolved mammal houses and nurtures the young in an especially evolved body cavity; then, after birth, gradually bridges the young to independent life by feeding it with the special mammary secretion. The dairy industry is, of course, based on the exploitation of this evolutionary mammary development.

This type of reproductive method develops family life. Family life is also strong in many bird species, especially those like pigeons, which produce "crop milk", and as previously noted on a different organizational level, in social insects. But it is, perhaps, on the highest level in mammals, particularly in man, who is distinguished from other mammals by a higher level of consciousness and by the ability to raise children of different ages simultaneously. Thus a special type of social life evolves, leading to the development of the uniquely human social characteristics of patience, forbearance, and charity on the part of the older and stronger children toward the younger and weaker These newly evolved characteristics may be called moral or ethical, and are destined to play an ever greater part in the evolution of human social life if the human species is to survive.

In man we see the family idea, with its higher level of conscious homeostasis, develop into ever larger aggregations—tribe, clan, nation, and finally, perhaps, a world federation. These broader human aggregations are made possible by the unique human ability for abstract thinking and communication in symbolic terms—language. By such communication men learned to recognize, in an impersonal way, the relatedness of all mankind. These unique recognition qualities in man have a structural basis in his nervous system. Primitive animals and primitive functions in higher animals are controlled by the autonomic nervous system concerned primarily with adjustment between organs within the individuals; the higher functions in the more evolved animals are controlled by the central nervous system, especially by the brain and more particularly by the forebrain, the cerebral cortex, concerned with adjustment of the organisms as a whole to distant environment. The development of the brain reached enormous proportions in man with correspondingly far-reaching recognition qualities. The brain weight (by no means the only index of high development) in a 150-lb man is over three pounds, whereas that in 1500-lb cattle is less than one pound (Ch. 17). Indeed, with the exception of the whale and elephant, man has the largest absolute brain. (Fig. 10.1).

The extraordinary brain development in man and his unique abstract or symbolic method of communication and preservation of accumulated knowledge, introduced a new factor in evolution, not dependent exclusively on genetic modification. The genetic make-up of man is certainly the same today as it was 200 years ago—and perhaps 20,000 years ago—and yet what transformations have occurred in human life, due to the development of science! Indeed, the automobile, telephone, electric light, radio, hydroelectric power, airplane, submarine, bombers, poison gases, not to speak of the gang plow and tractor, cream separator, combine harvester, chemical fertilizers, immune sera, anti-toxins, prefabricated houses, and so on, developed within the writer's memory. The evolution and integration of human society has thus become disengaged from genetic change, although it may lead to *purposive* genetic change. The future course of the evolution of man is in the hands of man himself, and it is difficult to predict what he will do with himself.

His future becomes ever more unpredictable by the very development of his abstract methods of thinking and communicating and by his science and invention. Thus an abstract idea, perhaps biologically destructive and therefore humanly senseless, if rationalized in words which appeal to emotional residues, may precipitate a world war and all but destroy man and his works. World War I is said to have cost in goods the equivalent of 340 billion dollars and some 33 million human lives in military and civilian casualties. The present better and bigger World War II, it is estimated, will cost at least the equivalent of 1000 billion dollars in goods and 50 million in military and civilian casualties. And who can predict what the third world war will cost and whether human society will react to these changes "so as to bring itself to normal"?

This calls attention to a curious characteristic of the average man: that while he thinks himself logical enough to have "common sense", he is often devoid of it. It took not the "common sense" of the average, but the uncommon sense of the rare "impractical" scientist to demonstrate that the earth is not flat, and so on for nearly every astronomic and other scientific discovery. Words, or language, may be used for illogical as well as for logical ends. This is generally known to psychologists.

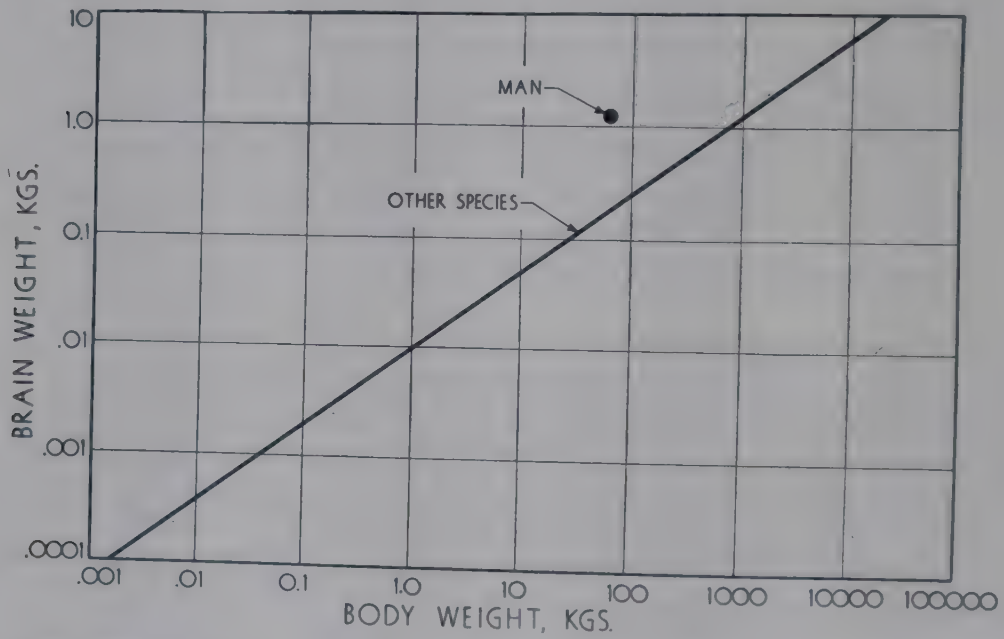

Fig. 10.1 The relation between the average brain weight of mature man and of the average brain weight of mature mammals of other non-anthropoid species ranging from mice to whales. Man's brain weight is almost as large as the elephant's.

Most of us are, indeed, familiar with "psychologic warfare", the "war of nerves",[60] and with the concept of "rationalization". Like other human inventions, language may be used for good or evil, for healing or for wounding, for peace or for war[60, 61].

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[60] For psychology and propaganda as war weapons, see among others, Cantrill, H., "The Psychology of Social Movements," New York, 1941. Pope, A. P. (Chairman), "German Psychological Warfare," Committee for National Morale, 51 E. 42nd St., New York, 1941. Hacket, F., "What Mein Kampf means for America," New York, 1941.

[61] There is a growing literature on non-logical thinking. For the most elaborate book on non logical patterns of human action, one which may have encouraged the rise of Fascism and Nazism, see Vilfredo Pareto, "Traité de sociologie générale," Paris, 1917, or Pareto, V., "The mind and society," New York, 1935. For more recent books, see among others, Korzybski, A., "Science and Sanity," The Science Press, 1933; Baynes,

Social homeostasis in man, as it relates to the balance between peace and war, appears to be roughly as follows[62, 59]. Animal evolution, including that of man, involves two opposing drives: (1) an egoistic (strutting, fighting, various "pecking-orders"[62], and other forms of egocentric self-aggrandizement) and (2) an altruistic (sex, parenthood, family, flock, herd, tribe, clan, nation, and perhaps supernation, and other forms of sociocentric activity).

Allee[62] and colleagues[8] emphasized the relatively greater altruistic than egoistic drives in evolution; otherwise the more highly evolved animals and animal societies could not have evolved because the animals would have destroyed each other under the compulsion of the self-aggrandizement drive. This may have occurred in some species that developed particularly effective fighting weapons (as saber teeth in the saber-tooth tiger), and this may be the case in contemporary man with his scientific weapons[63].

Paralleling the development of man's increasing powers for destructive warfare, as a result of his thinking on abstract levels, there also developed in all human civilizations a unique altruistic power on an abstract level, one which goes under the general name of "religion". Omitting for the present purpose the ritual and supernatural aspects of religion (without, however, minimizing their importance as carriers of altruistic action), its basic features are humility, counteracting the strutting and related self-aggrandizement drives, and neighborliness or the Golden Rule, counteracting the fighting and related pugnacious drives.

These two basic features of all religions, no matter how worded, are generally accepted not only by the leaders of conventional religious sects but also by philosophers and biologists who have outgrown the stage of so-called conflict between science and religion[64]. In brief, it appears that religion is a social homeostatic phenomenon evolved on a characteristically human level of symbolic thought, as war is evolved on a characteristically human level of abstraction. This homeostatic mechanism, religion, has not been functioning well in recent years, and it is suggested that it be investigated on the characteristically human level, scientifically, to set it aright, so as to serve its function in keeping in check destructive forces in the form of world wars. The greatest immediate need seems to be the development of methods for selecting leaders who will utilize the tools of science, which grow cumulatively ever more powerful, for peaceful construction rather than for warlike destruction.

10.10: Notes on organismic or field theory and on research methods. The living body's building stones, the electrons, protons, atoms, and molecules, are no different from those in non-living systems. But in virtue of its peculiar

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H. G., "Germany Possessed," London, 1942. Brickner, R., "Is Germany Incurable?" Lippincott, 1943. Stuart Chase, "The tyranny of words," 1938. Woolf, L., "Quack, Quack," Harcourt-Brace, 1935. Ogden, C. K., and Richards, I. A., "The meaning of meaning," Harcourt-Brace, 1936. Richards, I. A., "The philosophy of rhetoric," Oxford Press, 1935. Schiller, F. C. S., "Formal logic," Oxford Press, 1935. Bridgman, P. W., "The logic of modern physics," Macmillan, 1932.

[62] Allee, W. C., *Science*, **97**, 517 (1943).

[63] Kettering, Charles F., "You chemists are more or less responsible for this war", *Chem. and Eng. News of the A.C.S.*, **21**, (1943).

[64] A. N. Whitehead, philosopher and mathematician, writes: "Science is concerned with the conditions which regulate physical phenomena, whereas religion contemplates moral and aesthetic values. On one side there is the law of gravitation; on the other, the contemplation of the beauty of holiness". W. C. Allee, a biologist, states: "To me 'God' is a . . . name for the personification of all the best that the human race has been able to think and do and of all the beauty we have created, together with all the natural beauty we can appreciate; and religion as . . . unselfish living and honest thinking. . . ." To the author[59], religion seems best defined by: the consecrated devotion to the values and/or to the faiths which seem to promote the best interest of humanity.

organization the *organism as a whole* is in a different category from that of non-living systems[65]. In general, the biological form of order is different from those found in non-biologic systems—"it is a new dialectic order"[66].

The organismic or field hypothesis in biology[67] is similar in intent to the field theory of the newer physics. Just as the "field" in physics is an electromagnetic integrative process, so the "field" in biology is an integrative process binding the many components into a whole, perhaps at different levels (Ch. 17). The characteristic of the *field pattern* as defined by Weiss is that *it tends to be restored on disturbance*, which is also the definition of homeostasis.

The existence of a stable field pattern during growth and development may be demonstrated experimentally. It was pointed out (Chs. 7 and 16) that an egg, or even a gastrula, may be divided into several parts, and that each part may develop into a complete individual. This indicates that the destinies of the parts of the embryo are also shaped by the environment, and by the field pattern which restores itself after being cut up into parts. This was substantiated in another way by Spemann, who demonstrated that prior to the gastrula stage head formation may be induced in either head or tail region under the influence of a hormone-like head organizer, or under the influence of another field, by transplantation (see Sect. 7.8.2).

In a later stage, however, tissues no longer respond indiscriminately to *organizers*; each tissue develops a characteristic response, and the formation of head or tail depends not only on the nature of the organizer, but also on that of the tissue competence. Thus, at first, any part of the neurula could develop gills; later only a special gill area is capable of developing gills.

These ideas on individual (ontogenetic) loss of plasticity with advancing age may be extended to species (phylogenetic) loss of plasticity with advancing evolution. Primitive organisms have greater potentialities for diversification than more evolved forms; a given species is such not because it was evolved from a given evolutionary predecessor but because, in addition to the proper potentialities of the predecessor for the given type of evolution, the predecessors were subjected to environmental influences and field structures which acted as "evocators" or "organizers" for the given evolutionary course of the species (see Sect. 7.8.1).

As growth proceeds and the tissues and organs become ever more specialized, they necessarily become further separated from one another in space and time because of the differential rate of aging of tissues and organs. The various specialized organs are, however, closely integrated by organismic devices, such as the nervous, circulatory, endocrine and other systems.

What was said about ontogenetic specialization and spatial separation is applicable to phylogenetic specialization and spatial separation, with consequent greater need of integration by increasingly complex organismic devices.

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[65] Frank, L. K., *Philosophy of Science*, **2**, 210 (1935).

[66] Needham, J., "Order and life," New Haven, 1936.

[67] Burr, H. S., and Northrop, F. S. C., "The electro-dynamic theory of life," *Quart. Rev. Biol.*, **10**, 322 (1935); *Growth*, **1**, 78 (1937).

Schmalhausen[68] remarked that the greater the degree of specialization of parts of an organism, the greater the degree of their interdependence and the higher the integration level. High specialization of structures and functions must necessarily be associated with high organismic integration if the organism is to survive. The same idea was expressed by many others.

Since a highly specialized organism is a closely interrelated field-structure, it follows that when a tissue, cell, or molecule is removed from its field, it no longer exhibits its normal "organismic" characteristics[65]. Consequently, the usual method of experimental investigation of growth is in a sense artificial because it separates the unified growth process. Experimentally, however, the whole is often best approached through a study of its parts. The study of parts often leads to valuable intellectual syntheses of the whole[69]. Such, in fact, is the history of many scientific syntheses. The configuration of the atom as a whole was learned by splitting it into parts. The discovery of many vitamins and hormones and of their interrelations was accomplished in some respects by artificial "split-field" methods. The "split-field" method of research may be philosophically objectionable, but in practice it is unavoidable.

Other methodological problems have been raised since the development of the field, organismic, and relativity concepts, indicated by the following illustrations.

One of these is known as the *principle of uncertainty* or *indeterminancy* formulated by Heisenberg[70] in 1926, to the effect that the observed system is altered by the observation of the observer.

This Heisenberg Principle was formulated for small-scale (*e.g.*, motion of electron) events. To illustrate, an electron is observed with the aid of the light of another electron. This light influences to an unknown extent the behavior of the observed electron, so that it is impossible to observe a given electron unaffected by the observation light. That is to say, the observer is a part of the observed system, and the measured object is altered by the act of measurement itself.

This principle, based on small-scale observations, may be extended to large-scale observations whenever the act of observation alters the measured object. Thus it is not possible to determine the precise chemical constitution of a *living* cell, inasmuch as the attempt of the observer to observe the cell (by chemical analysis) alters the observed system (by killing it). Of course, this is rather an extreme example.

The application of Heisenberg's deductions from small-scale events (electrons, protons) to large-scale events may be illustrated more cogently by examples from Compton[70] and Lillie[71]. Nerve impulses, electrochemical in nature, are small-scale events, as, for example, those resulting from the impingement of light protons on the eye. The organism acts as a powerful amplifier which sets in motion large-scale events. Consequently, the large-scale end-result may have uncertainties of the same order as the small-scale events.

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[68] Schmalhausen, I., *Quart. Rev. Biol.*, **14**, 65 (1939).

[69] *Cf.* Hopkins, F. G., *Science*, **78**, 219 (1933).

[70] Heisenberg, W., "The physical principles of quantum theory," Univ. Chicago Press, 1930. Compton, A. H., "The freedom of man," New Haven, 1935.

While the behavior of small-scale events at a given moment is not definitely determined, it obeys the laws of probability. "The quantities which appear in its [quantum mechanics] laws make no claim to describe physical reality but only the probability of the appearance of a particular event" (Einstein). This generalization is in a sense applicable to all measurements and predictions, which is one reason for the use of statistical methods in the analysis of experimental data.

Large-scale uniformities, which constitute the subject matter of scientific laws, may be considered as statistical averages of small-scale or "atomic" diversities. Thus, while it is not possible to predict individual durations of life, yet, judging by the practical success of life insurance companies, it is possible to predict the *average* expectation of life. The immense practical success of science and industry based on scientific laws testifies to the *average* orderliness of events. In view of this evident orderliness, the following unqualified opinion[72] seems misleading. "The universe is . . . without unity, without continuity, without coherence or orderliness . . . . Order, unity, and continuity are human inventions just as truly as are catalogs and encyclopedias . . . . Such orderliness as we appear to find . . . seems to be due to our passion for pigeon holes, and it is quite doubtful whether there are such things as laws of nature". The view that the world is an *interrelated* dynamic configuration seems more reasonable. Perhaps the following remark by Hyman Levy represents more nearly the situation: "The world is an enormous interrelated dynamic muddle with intermittent patches of order and sanity".

The problem of uncertainty discussed above leads to the problem of the methodology of mathematical analysis of experimental data.

Now mathematics has two aspects: theoretical, not dependent on reality, and applied, which is very real indeed. The two aspects are illustrated by the following quotations and discussions.

"Mathematics is not science; it is not nature, unless it be in the nature of the mind; it is not concerned with the truth but only with the exactness of the deductive process. Is the formula 50 × 2 = 100 true or false? The answer depends on circumstances. It is true when applied, for example, to 50 apples in one basket and 50 in another. It is debatable when applied, for example, to temperature: 100° C is hardly twice 50° C".—E. Bidwell Wilson.

"Mathematics is a natural science . . . it has its origin in the objective world, of which it studies the spatial and numerical aspects. The law that 2 × 2 = 4 is not only a law on paper, but as a mathematical law expresses relations in objective reality, like the law that hydrogen and oxygen form water under proper conditions".—D. J. Struik.

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[71] Lillie, R., *Science*, **46**, 139 (1927).

[72] Russell, Bertrand, "What I believe," *Nation*, p. 412, 1940.

"One cannot escape the feeling that mathematical formulas have an independent existence and an intelligence of their own . . . that we get more out of them than was originally put into them".—Heinrich Hertz.

"One tries . . . to employ numerical discourse . . . because of the stock of ready-made devices and calculations which were accumulated in the pursuit of mathematics". —Leonard Bloomfield.

For our purposes, the usefulness of mathematics consists in its operational convenience. Mathematics is a lever, as it were, by the use of which unwieldly masses of experimental data are lifted into analytic view. The tremendous progress of the physical sciences in general and of engineering in particular since the Renaissance is in large measure due to applications of the analytic mathematical methods developed during this period. These methods should also prove fruitful in the investigation of motions of biological phenomena, such as growth.

The operational advantages and disadvantages of mathematics are not unlike those of symbolic logic[73]. Both have the advantages of simplicity, "purity", and isolation. But the advantages of generality, simplicity, purity, and isolation are also disadvantages. A symbolic language isolated from the material world cannot fully represent the complex phenomenal interrelationship of the material world, although it is probable, as indicated, for example, by the groupings of matrix algebra, that the symbolic language of mathematics and logic will develop a broader adequacy reflecting physical reality to a greater extent. Regardless, therefore, of the technical refinements of a mathematical result, its representation of a situation is necessarily inadequate and over-simplified, and must be interpreted in the light of what is called "common sense", that is, judgment in the light of experience.

In connection with the widespread application of the mechanical rules of statistics to biology, Wilson[74] writes: "I say beware of the mere formal application of probable error to meager statistical material. Your conclusions will almost certainly be wrong. The statistical method, like other methods, is not a substitute for, but a humble aid to the formation of a scientific judgment. Only with this philosophy in mind may we truly hope, with care, to avoid in the main being classed in the superlative category of that oft-cited sequence of liars, damned liars, and statisticians!"

Sets of observations, for example, basal metabolism and body weight (Chs. 13 to 15), are usually related to each other by some equation. The equation may be empirical or rational. There are many degrees of rationality, but the constants of the rational equation should at least have definitness of meaning. A potential series, such as $Y = a + bX + cX^2 + dX^3 \ldots$, is not rational because (1) any continuous set of observations can be represented by such a series if enough terms are chosen, and (2) if one of the terms of the series is omitted, the remaining constants assume different numerical values. This type of equation is, therefore, ambiguous because its terms have no definite, constant, meaning.

An empiric equation, then, may have description value, but does not represent a uniformity of nature. A rational equation, such as the gas law $PV = NRT$, or the gravitational equation $F = G(MM^1/d^n)$, represents a certain concept of the phenomenon, perhaps idealized, that is, undisturbed by lesser causes, the constants of which are unambiguously defined. Rational equations often represent the data with less precision than empiric, because of their idealization. On the other hand, a prediction based on a rational equation is more reliable. The distinguishing feature of the rational equation is not that it represents data with great precision, but that it represents or intends to represent a uniformity or "law" of nature.

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[73] *Cf.*, Neurath, Bohr, Dewey, Russell, Carnap and Morris, "International Encyclopedia of Unified Science. Foundations of the Unity of Science", Vol. 1, No. 1, University of Chicago Press, 1939. Woodger, J. H., "The technique of theory construction," *Id.*, Vol. 2, No. 5.

[74] Wilson, E. Bidwell, *Science*, **80,** 193 (1934); **58,** 93 (1923); **63,** 289 (1926); **65,** 581 (1927).

Equations frequently have broader significance than the author believes them to have, so that they can represent with equal facility quite different, even contradictory, theories. Likewise, different types of equations may often represent the same phenomenon. There is, therefore, no dividing line between rational and empiric equations except in the author's concept.

In the last analysis, mathematical representations are oversimplified mathematical models, only partial descriptions of a limited portion of a long chain of interrelated events, rather than explanations. This is due to the discrepancy between the necessarily idealized nature of the assumptions for mathematical representation on the one hand and the complexity of the "field" or the process on the other. A mathematical equation represents an isolated relationship while reality is organismic, with complex multi-dimensional ramifications. Rationalism and empiricism are, therefore, relative terms, descriptive of the spirit of the investigator.

Empiric equations are useful for condensing unwieldy tables into a brief formula, for codification (*e.g.*, formulating growth standards), classifications (*e.g.*, with regard to rate of growth and development, variability, correlation, etc.), but not for predicting outside the observed limits. Agriculturists are familiar with the practical usefulness of age and other time "standards" of physical growth, milk production, egg production, wool production, fertility, life expectancy, and so on.

10.11: Summary. This chapter is concerned with a very general principle in biology, designated "homeostasis" by Cannon, which may be called the principle of Claude Bernard for living systems analogous to the principle of Le Chatelier for non-living systems.

Homeostasis, or the principle of Claude Bernard, refers to the regulatory mechanisms which maintain constant the "internal environment" of the organism in the face of changing conditions. Thus the body temperature of man remains constant although the external environmental temperature may range from 0°F to 100°F; high-milking dairy cows gain (from the feed) or lose (into the milk) colossal amounts of minerals, proteins, carbohydrates, and water, yet maintain constant the concentration of these nutrients in the blood; and so on.

Homeostasis is the major manifestation of what is sometimes referred to as the "field" formulated by the "organismic theory" in biology. "Field" refers to the totality of the interactions in the living system with the environment, internal and external. The *living field* pattern of the biologist is analogous to the *electromagnetic field* pattern of the physicist. The behavior of the bodily constituents is determined by the living field structure as a whole in the same sense as the behavior of iron filings or of electric events is determined by the electromagnetic field structure as a whole. This living field pattern has a certain dynamic stability, that is, it tends to restore itself to "normal" by many organismic or homeostatic devices.

These concepts of field, organism, and especially homeostasis, were extended to societies of organisms, especially to their ever finer social integration in the course of evolution; and to certain philosophic aspects in sociology and social evolution. Human society is apparently in the throes of a transition period due to the unbalanced development of techniques, discussed in the text (also in Ch. 25).

The concepts of field and homeostasis invalidate the concept of "cause" as a one-sided action. Thus many endocrines are stimulated to activity by the pituitary (tropic hormones). But this is not one-sided; the glands which are controlled by the pituitary also control the pituitary. The interrelation is mutual. Moreover, the pituitary is, itself, a part of the total functioning organism, and can function only as the organism keeps it so. Similarly in other realms: high government expenses "cause" high taxes; and high taxes "cause" high government expenses. The interrelation is mutual.

The field concepts of living and non-living systems may be integrated into a more general field concept. There is no sharp dividing line between living and non-living, but they function at different levels, just as within the living category, there are many different levels of organization and function.

The narrow border between living and non-living, at its limit, is indicated by the fact that *crystalline* protein ("non-living") prepared from tobacco-mosaic virus has the ability to proprogate itself ("living")[75]. The bacteriophage[76] is in the same category.

During growth and development the "field" is thought of as an integrative *process* which organizes the diverse elements into an integrated unit. The structure has many categories—atoms, ions, molecules, cells, organs, organ systems; but these structures, at different levels of complexity, function together harmoniously as part of the "field". The living field is stable, yet its stability is not static but dynamic. Thus protoplasm is chemically very unstable, but an organism like a man may function in the same recognizable individual form for a century. The individual atoms and molecules are undergoing continuous change, but the pattern, the "field", remains until a limiting homeostatic mechanism breaks down and the organism dies.

The principle of homeostasis is illustrated in the text by many examples, earthy and theoretical. Indeed every chapter in this book is an illustration of this principle. It is an extremely useful one in biology; like the theory of evolution, it binds scattered facts, apparently unrelated and confusing, into a sane whole.

General comments are presented on the use of mathematics in biology, with special reference to the relative significance of rational and empirical equations.

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[75] Vinson, C. G., *Bot. Gaz.*, **87** (1929); *Phytopathology*, **22**, 965 (1932); Univ. Missouri Agr. Exp. Sta. Res. Bull., 237, 1936. Stanley, W. M., *Science*, **81**, 644 (1935).

[76] D'Herrelle, F., "Bacteriophage and its behavior", Baltimore, Md., 1926.

Chapter 11

Homeothermy, Temperature in Life Processes, and Productive Efficiency

> Uniformity of the internal environment is the condition for free and independent life. *Claude Bernard*
>
> Homoiothermicity . . . was bound to arise in . . . animal life tending to free itself from the domination of the inorganic. *Joseph Needham*

11.1: Introduction. Feathers, fur, and hair, which one phase of animal husbandry cultivates, serve the animal wearer in essentially the same way as they later do the human wearer. They are aspects of *physical*[1] temperature-regulation in warm-blooded animals or *homeotherms*. Homeotherms also employ *chemical*[1] temperature-regulating mechanisms, involving metabolic changes, to keep the body temperature constant.

The larger homeotherm finds no need of an annual migration to avoid reasonably low temperature. Many small homeotherms, especially small birds, migrate seasonally because they have a relatively larger surface area in comparison to body weight than do large animals and heat loss is proportional to surface area (Chs. 13, 17). The geographic distribution of animals is thus dependent on body size, that is, on the ratio of surface area to body weight, and on other factors. Geographic distribution, efficiency, and profitableness of farm animals of different size is likewise dependent on temperature and other geographic conditions.

Cold-blooded animals, or *poikilotherms*, whose body temperature fluctuates with that of the environment, are evidently more dependent on outside temperature than homeotherms. While the rate of living of homeotherms is approximately the same throughout the year, that of poikilotherms varies with latitude and temperature (Ch. 8). When the environmental temperature falls to freezing, their body cells freeze, causing death. Small poikilotherms, therefore, descend below the frost line seasonally, to the lower depths of water, mud, or soil or, like some insects, migrate to warmer climates.

[1] Other *physical* heat-regulating mechanisms: moisture vaporization from skin (sweating) and lungs (panting); moving of blood to surface (for cooling in sweating species) or to interior; layers of fat for insulation against cold; huddling, looking for shelter, for warm sun, for cool shade, etc. *Chemical* temperature regulation: changing metabolic rate by various devices, such as shivering, changing muscle tension, increased adrenaline and thyroxine production, and so on.

Poikilotherms which cannot thus migrate often perish. Some very small poikilotherms desiccate and encapsulate for protection.

The disappearance of the great reptiles in the Cretaceous and Eocene periods is often attributed to unusual temperature changes which permitted homeotherms, but not poikilotherms, to survive. Strange as it may seem, some homeotherms (the sweating species) also stand higher temperature better than some poikilotherms.

Homeothermy has many aspects, theoretical, agricultural and engineering. The theoretical aspect is concerned with homeothermic mechanisms; the agricultural, with the influence of environmental temperature and humidity on productivities and efficiencies of farm animals; the engineering, with ventilation, heating and cooling (air conditioning). We shall discuss each of these; the theoretical and numerical discussions are presented in small type, the practical and general in large type.

Homeotherms may be divided into several classes according to body temperature,[2] which ranges from about 36° C (96° F) in elephants to about 43° C (109° F) in small birds. In general, the rectal temperature of mammals is about 38° C (100° F) and of birds, 4° C higher, namely, 42 to 43° C (107–109° F). It is, however, about 37° C (98.6° F) in man. Typical rectal temperatures: cattle 101° F (38.5° C), horses 100° F (38° C), sheep 103° F (39° C), goats 104° F (40° C), swine 103° F (39° C), cat and dog 101.5° F (38.6° C), rabbit 103° F (39.5° C), chickens 107.1° F (41.7° C), goose 105° F (40.8° C), dove 41.8° C, rat 37.3° C, elephant 35.9° C, marmoset 37° C.

Rectal temperature classes:

36–38° C (96–101° F): men, monkeys, mules, asses, horses, rats and mice, elephants.
38–40° C (100–103° F): cattle, sheep, goats, dogs, cats, rabbits, pigs.
40–41° C (104–106° F): turkey, goose, duck, owl, pelican, vulture, bittern.
42–43° C (107–109° F): fowl, pigeon, turkey, quail, partridge, pheasant, English sparrow, bluejay, starling, bobwhite.

The higher mammals and birds are very sensitive to temperature increase in the body; a rise of only 3° C (5.4° F) above normal for some time in the adult may be fatal. The young are less sensitive.

The body temperature of chicks rises from about 39° C (103° F) the first day, through 40° C (104° F) the second day, 41° C (106° F) the third day, exact temperature depending on time of day measured (Fig. 11.5B).

When fowl eggs are incubated at 37.8° C (100° F) their temperature begins to rise by the sixth day—reaching about 40° C (104° F) by the eighteenth day of incubation.[3]

Egg temperatures of wild birds under natural incubation conditions are, on the average, 34° C (93° F), being 33.6° C for passerine birds, and 36.4° C for galliforms. A mallard nest with 18 eggs showed a difference of 12° C (22° F) between an egg in the center of the nest and one at the outer edge.[4]

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[2] Interesting references: Gerstell, R., and Long, W. H., "Physiological variations in wild turkeys", Pennsylvania Game Commission Res. Bull. 2, Harrisburg (1939). Baldwin, S. P., and Kendeigh, S. C., "Temperature of birds", *Sci. Pub. Cleveland Museum Natural History*, Vol. 3, 1932. Pearse, A. S., and Hall, F. G., "Homoiothermism—the origin of warm-blooded vertebrates", Wiley, 1928. Lamoreux, W. F., and Hutt, F. B., "Body temperature in the chick," *Poultry Sci.*, **18**, 70 (1939). Benedict, F. G., Carnegie Inst. of Washington Publ. 503, p. 63. Lee, A. C., "Temperature of the rabbit," *Am. J. Physiol.*, **125**, 521 (1939). Dukes, H. H., "Physiology of domestic animals," Comstock, Ithaca, 1942.

[3] Romanoff, A. L., *Science*, **94**, 218 (1941).

Some animals are intermediate between homeotherms and poikilotherms. Thus[5] the duckbill and Australian anteaters not only have the relatively average low body temperature of 25° C (77° F), but their body temperature changes by about 10° C with an environmental temperature change of 30° C.

11.2: Relative productivities and efficiencies of homeotherms and poikilotherms. In poikilotherms the speed of the life processes, such as feeding, growth, metabolism, aging, etc., increases with temperature up to a certain limit (depending on species) in accordance with the Van't Hoff law, just as the speed of inanimate reactions does. Since temperature probably affects the anabolic (productive) and catabolic (destructive, maintenance, aging) processes to an equal degree, the gross or overall energetic efficiency of the transformations is likely to remain unchanged. By the same reasoning, if all other conditions are equal, the gross energetic efficiency is likely to be the same in poikilotherms and homeotherms in spite of enormous body temperature and energy-metabolism differences. This is illustrated by Table 11.1 which shows that both maintenance cost and growth rate are enormously higher in warm-blooded animals (cat, dog) than in cold-blooded (Pike), with the net result that efficiency is apparently the same in both.

TABLE 11.1.—Time and maintenance energy expended for doubling body weight in homeotherms and poikilotherms. Data rearranged from Rubner.[6]

Doubling Body Wt.	Body Weight (gms)			Time required to double body wt. (days)			Maintenance energy expended (Metabolism) (Cals)		
	Cat	Dog	Fish (Pike)	Cat	Dog	Fish	Cat	Dog	Fish
"Birth Wt"	87	225	70						
1	174	450	140	8	10	270	3200	3000	3300
2	348	900	280	12	13	300	4000	3070	2350

The following data by Barthelemy and Bonnet,[7] cited by Needham, on frog's eggs up to disappearance of external gills confirm the above conclusion based on Rubner's data.

Temperature (°C)	Development time (days)	Gross efficiency (%)
9	30	75
11	22	73
14	20	75
21	8	75

Rahn[8] estimated that the maximal efficiency of energy utilization in growth is of the same order in the vertebrates, insects, and bacteria studied (see, however, Ch. 3).

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[4] Huggins, R. A., *Proc. Am. Soc. Zool.* (1939), 39th (Columbus) meeting.

[5] Martin, C. J., "Respiratory exchange in monotremes and marsupials," *Trans. Phil. Soc. London*, **195B**, 11 (1903).

[6] Rubner, M., *Biochem. Z.*, **148**, 222 (1924); **148,** 268 (1924).

[7] Barthelemy, H., and Bonnet, R., *Bull. Soc. Chim. biol.*, **8,** 1071 (1926).

[8] Rahn, O., *Growth*, **4,** 77 (1940).

According to Rahn's estimates, one Cal. of food produces the following Calories in body tissue: in pig, 0.2–0.4; trout, C.18–0.31; cockroach, 0.34—0.35; mold, 0.58–0.70; colon bacilli, 0.13–0.24; pseudomonades, 0.21–0.22.

Tyler[9] reported for eggs of some marine invertebrates, that the total oxygen consumed in reaching a given stage of development at different temperatures (7.5°, 10°, 12°, 15°, 20°, 22°, 25° C) was, with one exception, the same within the limits of error of the measurements; this occurred in spite of the fact that the speed of attaining the given stage increased rapidly with increasing temperature.

11.3: Temperature coefficients and the Van't Hoff-Arrhenius equation in life processes. A fascinating branch of biologic investigation is concerned with the search for analogies—even if they are empirical *form* analogies and gross oversimplifications—between the characteristics of given biologic processes and those of some inanimate process, such as that of an inorganic chemical reaction. Such analogies introduce order, and are often suggestive and practically useful. As part of this type of research a considerable literature has developed[10,13] on the applicability of the Van't Hoff[11] and Arrhenius[12] temperature-coefficient equations, formulated from thermodynamic reasoning for simple inorganic systems, on the rate of biologic processes.

The Van't Hoff rule in linear ratio form states that (within certain limits) the speed of chemical reactions is doubled or trebled, that is, increased by 200 to 300 per cent, for an increase of 10° C or 18° F in temperature, or is increased by 20 to 30 per cent for an increase in 1° C.

The above statement may be represented by the equation

$$Q_{10} = \frac{S_2}{S_1} = 2 \text{ to } 3 \tag{11.1}$$

in which Q_{10} may be called the Van't Hoff coefficient, and S_1 and S_2 represent the speeds of the process at temperatures $t°$ C and $(t + 10)°$ C.

Thermodynamic considerations indicate that the Absolute temperature scale should be employed and that the relation should be exponential rather than linear-ratio. Arrhenius[12], therefore, suggested the equation

$$S_2 = S_1 e^{\frac{u}{2}\left(\frac{T_2 - T_1}{T_2 T_1}\right)} \tag{11.2A}$$

in which S_2 and S_1 are the speeds (Arrhenius represented them by the reaction-velocity constants, K_2 and K_1) at Absolute temperatures T_2 and T_1; e is the base of natural logarithms, and the value 2, of course, represents the gas constant R (Ch. 2). In simple inorganic chemistry u is supposed to represent, in accordance with thermodynamic reasoning, the molecular heat of formation. In biology u is referred to as *temperature coefficient, thermal increment,* or *temperature characteristic.*[13]

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[9] Tyler, A., *Biol. Bull.*, **71**, 82 (1936).

[10] Loeb, J., *Arch. ges. Physiol.*, **124**, 411 (1908); *Sci. Monthly*, **9**, 578 (1919), and many other papers. Kanitz, A., "Temperatur und Lebensvorgänge," Berlin, 1915, and *Tab. Biol.*, **11**, 9 (1925); Matisse, G., *Arch. internat. de physiol.*, **16**, 451 (1921). Przibram, H., "Temperatur und Temporatoren im Tierreiche," Wien, 1923. Belehradek, J., *Biol. Rev.*, **5**, 30 (1930). Hoagland, H., "Pacemakers in relation to aspects of behavior", Macmillan, 1935.

[11] Van't Hoff, J. H., "Études de dynamique chimique," Amsterdam, 1894; Van't Hoff und Cohen, E., "Studien zur chemischen Dynamik," Amsterdam and Leipzig, 1896. Mellor, J. W., "Chemical statics and dynamics," London, 1915.

[12] Arrhenius, S., *Z. Physiol. Chem.*, **4**, 226 (1889).

By taking logarithms, ln, of (11.2A), we have:

$$\ln S_2 - \ln S_1 = \frac{u}{2}\left(\frac{T_2 - T_1}{T_2 T_1}\right) \tag{11.2B}$$

indicating that the applicability of this equation to data is easily determined by plotting[13] the logarithms of S against the reciprocals of T. Its applicability can also be tested by solving for u for several temperatures:

$$u = 2\frac{T_2 T_1(\ln S_2 - \ln S_1)}{T_2 - T_1} \tag{11.2C}$$

Arrhenius[14] suggested that when $T_2 - T_1$ is small, T_2T_1 is virtually a constant. Therefore, combining the two constants $u/2$ and T_2T_1 into one constant, c, we have:

$$S_2 = S_1 e^{c(T_1 - T_2)} \tag{11.3}$$

We prefer to write it simply, as

$$S = Ae^{kt} \tag{11.4A}$$

in which S is the speed of the process (as of growth, etc.) at ordinary temperature t; A is an empirical constant (value of S when $t = 0$); and k is the differential increase in relative rate of change (as of growth) for 1° C change in temperature. It is evident[15] from equations (11.2C) and (11.4) that $u = 2kT_1T_2$.

By taking logarithms of (11.4A),

$$\ln S = \ln A + kt \tag{11.4B}$$

The applicability of equation (11.4) to data is proved by the linear distribution on arithlog paper, and the value of k is the slope of the curve (times 2.3) of S against t. The value of k is 0.07 for a Q_{10} value of 2, meaning that the differential, or instantaneous, rate of change in speed, S, is 7 per cent per 1° C change in temperature. (The reason that the change in speed is 7 per cent for Q_{10} of 2 and not 10 per cent as given by the linear equation (11.1) is explained in Chs. 16 and 17.) This (our) method is understandable, as actual data are used, and k is the relative rate, or percentage rate when multiplied by 100, of increase in speed of the process per 1° C rise in temperature.

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[13] Crozier, W. J., *J. Gen. Physiol.*, **7,** 129, 189 (1924) **10,** 53 (1926) and other papers in this journal; also *Proc. Nat. Acad. Sci.*, **10,** 461 (1924).

[14] Arrhenius, S., "Quantitative laws in Biological Chemistry," London, 1915.

[15] Equation (11.4) may be written $K = \dfrac{\ln S_2 - \ln S_1}{T_2 - T_1}$.

For practical purposes the Van't Hoff Q_{10} rule, eq. (11.1), or a slight modification, as

$$Q_{10} = 1 + \frac{S_2 - S_1}{\frac{1}{2}(S_2 + S_1)} \times \frac{10}{t_2 - t_1}$$

is as good as the Van't Hoff-Arrhenius equation (11.2) because the maximum temperature range in biology—from 0° C to 40° C—is relatively insignificant in Absolute-temperature terms; and the temperature range for homeotherms is only a few degrees. Moreover, as the centigrade-temperature zero happens to coincide with the "physiological zero",[16] it seems to be the logical one to use.

Equation (11.2) is not applicable to the entire temperature range 0 to 40° C. but only for narrow segments, depending on the species of animal or rather, perhaps, on the enzyme which happens to be the limiting factor in a given temperature range. Moreover, as the temperature rises, the enzymes begin to be injured, that is, they tend to become denatured as proteins do,[17] with the net result that the accelerating effect of temperature on the speed of the limiting process may be counteracted by the inactivating effect on the limiting enzyme in the limiting process.[17] The change in speed of the process may, therefore, vacillate, or perhaps remain constant, for some temperature interval, and then decline. This may be the explanation of the peculiar "breaks" in the log speed $-1/T$ functions reported by Crozier and others; hence the linearity of the functions for narrow segments only, the lengths of the segments and the position of the "break" depending on the nature of the limiting enzyme and limiting process.

The fact that the speed-temperature curve breaks up into short segments reduces the significance of the question as to whether or not the relation is linear or exponential because either one can be "fitted" equally well to a sufficiently short segment. However, the numerical value of u in the Arrhenius equation (11.2) or of Q_{10} in equation (11.1) may be significant within appropriate temperature limits.

The above comments on biologic applicability refer to poikilotherms. The Van't Hoff-Arrhenius equation is less applicable to homeothermic processes because, by definition, homeothermy is a regulation which tends to keep the temperature constant in spite of fluctuations in environmental temperature. Thus, increasing environmental temperatures does not necessarily increase metabolism and body temperature, as would be expected from the Van't Hoff law; but it may stimulate the operation of counteracting mechanisms

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[16] Krafka, J., "The physiological zero," *J. Gen. Physiol.*, **3**, 659 (1921). Edwards, C. L., "The physiological zero and egg development," *Am. J. Physiol.*, **6**, 351 (1901). For developing hens' eggs the "physiological zero", at which development just begins is about 20° C (68° F).

[17] Chick, H., and Martin, C. J., "Heat coagulation of protein," *J. Physiol.*, **40**, 604 (1910); **43**, 1 (1911); **45**, 61 and 261 (1912). The Q_{10} for denaturation of protein is not 2 or 3, but about 15. The Q_{10} for coagulation of egg albumin is several hundred.

(increased sweating and vaporization, so as to keep the body temperature constant). However, as demonstrated in Section 11.5, the Van't Hoff rule often applies to the counteracting process, *e.g.*, to increase in respiration and

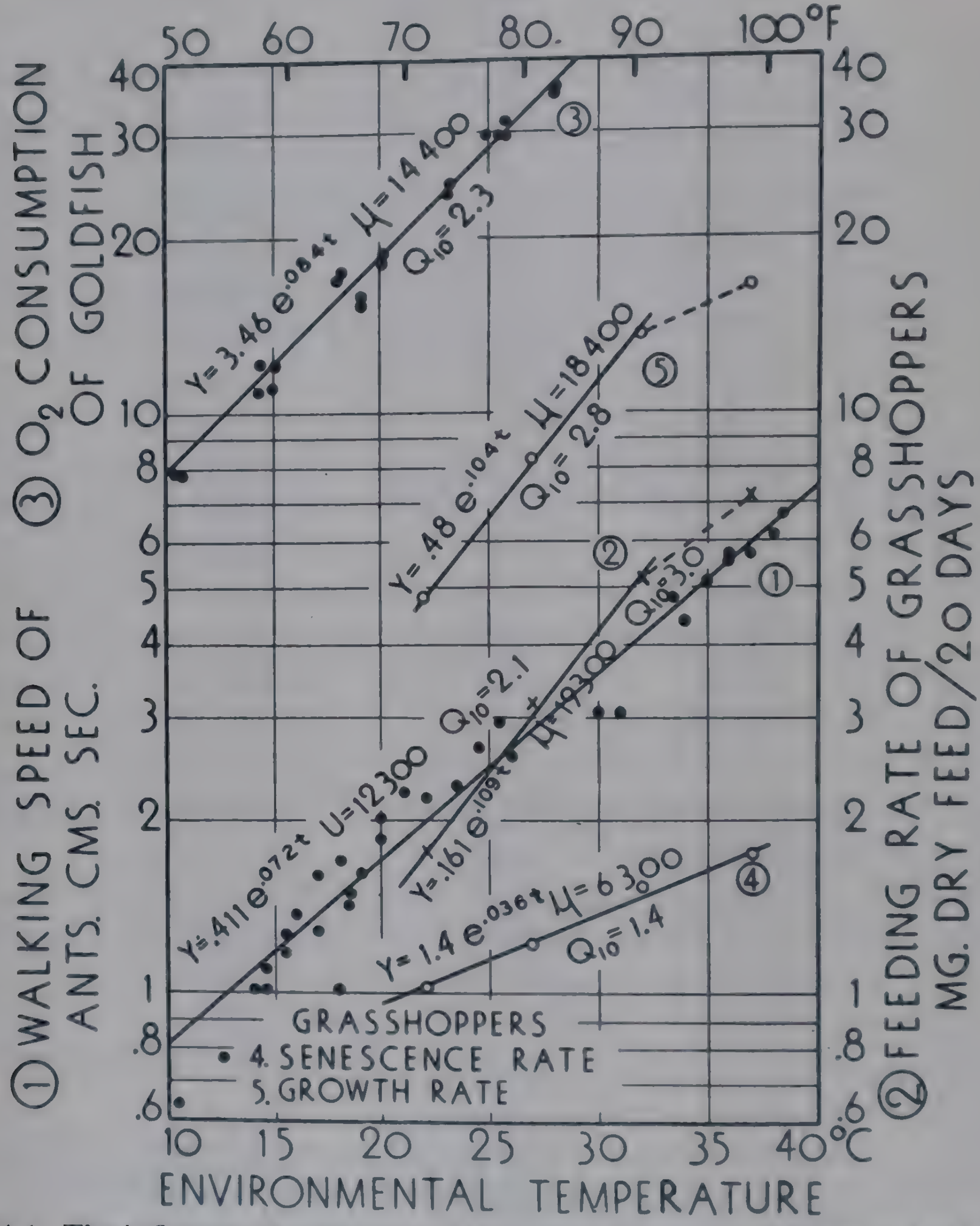

Fig. 11.1. The influence of environmental temperature on walking speeds of ants (1), feeding rate of grasshoppers (2), O_2-consumption rate of goldfish (3), aging rate (reciprocal of mortality rate) of grasshoppers (4), growth rate of grasshoppers (5). The Q_{10}, the *u* values, and equations were fitted by us to data on grasshoppers (by J. R. Parker, Univ. Montana Agr. Exp. Sta. Bul. 223, 1930), ants [by H. Shapley, *Proc. Nat. Acad. Sci.*, **6,** 204 (1920)], goldfish [by R. Egg and A. Krogh, *Rev. hydrobiologie*, **6,** 48 (1914)]. The Q_{10} for growth (5) and feeding (2) is nearly the same, 2.8 and 3, while the Q_{10} for aging (4) is only 1.4, meaning that the limiting reactions of the two processes are distinct. The Q_{10} of walking ants (1) is 2.1, of O_2 consumption in goldfish 2.3.

perspiration rate with increasing environmental temperature (Figs. 11.7 to 11.10).

Fig. 11.1 illustrates the influence of environmental—and consequently body—temperature, within the given limits, on the rates of *poikilothermic* processes. The linear distribution of the data on the arithlog grid indicates that the Van't Hoff-Arrhenius equation is applicable to the given processes. Increasing temperature by 10° C increases: the walking speed of ants 2.1 times ($Q_{10} = 2.1$), the metabolic rate of gold fish 2.3 times, the senescence rate 1.4 times and the growth and feeding rates of grasshoppers 2.8 to 3 times. (Note that the growth rate is increased twice as much as the senescence rate, a fact that may be of significance in geographic differences in population density.)

Summarizing, within rather narrow limits, the speed of biologic processes tends to increase with body temperature in the same manner as in inanimate chemical reactions. The literature and computational methods are discussed briefly.

11.4: Age changes in homeothermy. As Cannon has remarked, homeothermic mechanisms are not required by the developing mammal before birth. At birth and thereafter, however, survival becomes increasingly contingent upon the exercise of these mechanisms, and so poikilothermic embryos develop into homeothermic adults.

An important adaptation to environment is that birth or hatching under natural conditions occurs during seasons when the environmental temperature is optimal (Ch. 8), thus allowing time for development of homeothermy. Depending on environmental temperature, the body temperature in children[18] stabilizes (becomes fully homeothermic) between the first and second years; in rats[19] in about three weeks (Fig. 11.5), in domestic fowl and chicks,[20] in three to four weeks (Fig. 11.5), and so on.[21]

Since a knowledge of the influence of incubation temperature is important in agriculture, we investigated the applicability of the Van't Hoff law to the speed of growth of chick embryos at various incubation temperatures.[22] The results are presented in Figs. 11.2a, 11.2b, and 11.3. Fig. 11.4, plotted from data by Romanoff[23], indicates the influence of environmental temperature on hatchability, survivorship after hatching, and crippling when incubated at low non-lethal temperatures. It is evident that early growth and development in the chick can occur only within a very narrow temperature zone.

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[18] Kleitman, N., Titelbaum, S., and Hoffman, H., *Am. J. Physiol.*, **119**, 48 (1937).

[19] Gulick, A., *Am. J. Physiol. Proc.*, **76**, 206 (1926), and **119**, 322 (1937). Brody, E. B., *Am. J. Physiol.*, **139**, 230, (1943).

[20] Pembrey, M. S., Gordon, M. H., and Warren, R., "Response of chicks before and after hatching to changes of external temperature," *J. Physiol.*, **17**, 331 (1894–5); Simpson, S., "Body temperature of the domestic fowl during incubation," *Trans. Roy. Soc. Edinburgh*, **47**, 605 (1911). Kleiber, M., and Winchester, C. F., "Temperature regulation in baby chicks," *Proc. Soc. Exp. Biol. Med.*, **31**, 158 (1933); **38**, 793 (1938); also *J. Agr. Res.*, **57**, 529 (1938). Scholes, J. C., and Hutt, F. B., Cornell Agr. Exp. Sta. Memoir, **244**, 1942.

[21] Stier, T. J. B., and Pincus, G., *J. Gen. Physiol.*, **11**, 349 (1927–28). Pincus, G., Sterne, G. D., and Enzmann, E., *Proc. Nat. Acad. Sci.*, **19**, 729 (1933).

[22] Henderson, E. W., and Brody, S., Univ. Missouri Agr. Exp. Sta. Res. Bull., 99, 1927; Henderson, E. W., *Id.* Res. Bull., 149, 1930.

[23] Romanoff, A. L., Smith, L. L., and Sullivan, R. A., Cornell Univ. Agr. Exp. Sta. Memoir, 216 1938. Romanoff, A. L., *J. Agr. Sci.*, **25**, 318 (1935).

The age curve of growth in weight of the chick embryo (Figs. 11.2 and 11.3) appears to be composed of several segments, and temperature affects each of these segments differently. The data appear to follow the Van't Hoff law in the stages of growth preceding the normal 13-day stage, when $Q_{10} = 2$ to 3. Within the limits of 37° C and 41° C, the lower the temperature the higher the value of Q_{10}. Following the normal 16-day stage, the speed of growth is repressed by both higher and lower temperatures.

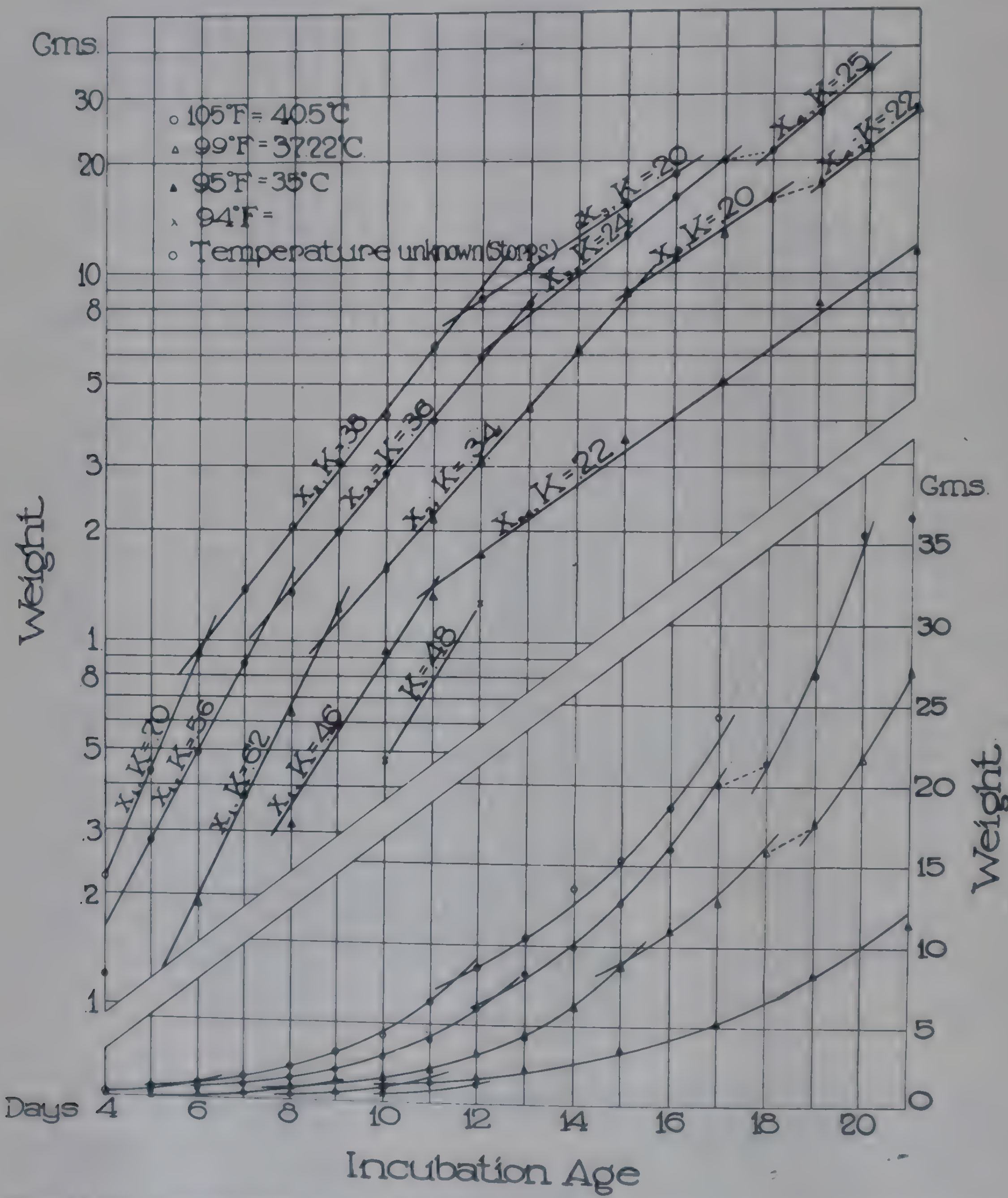

Fig. 11.2a. Growth of the chick embryo in wet weight at three temperatures

The historically interesting literature on the influence of temperature on the chick embryo has been reviewed by Needham[24], Romanoff and others. A few of these may be

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[24] Needham, J., "Chemical embryology," 1931.

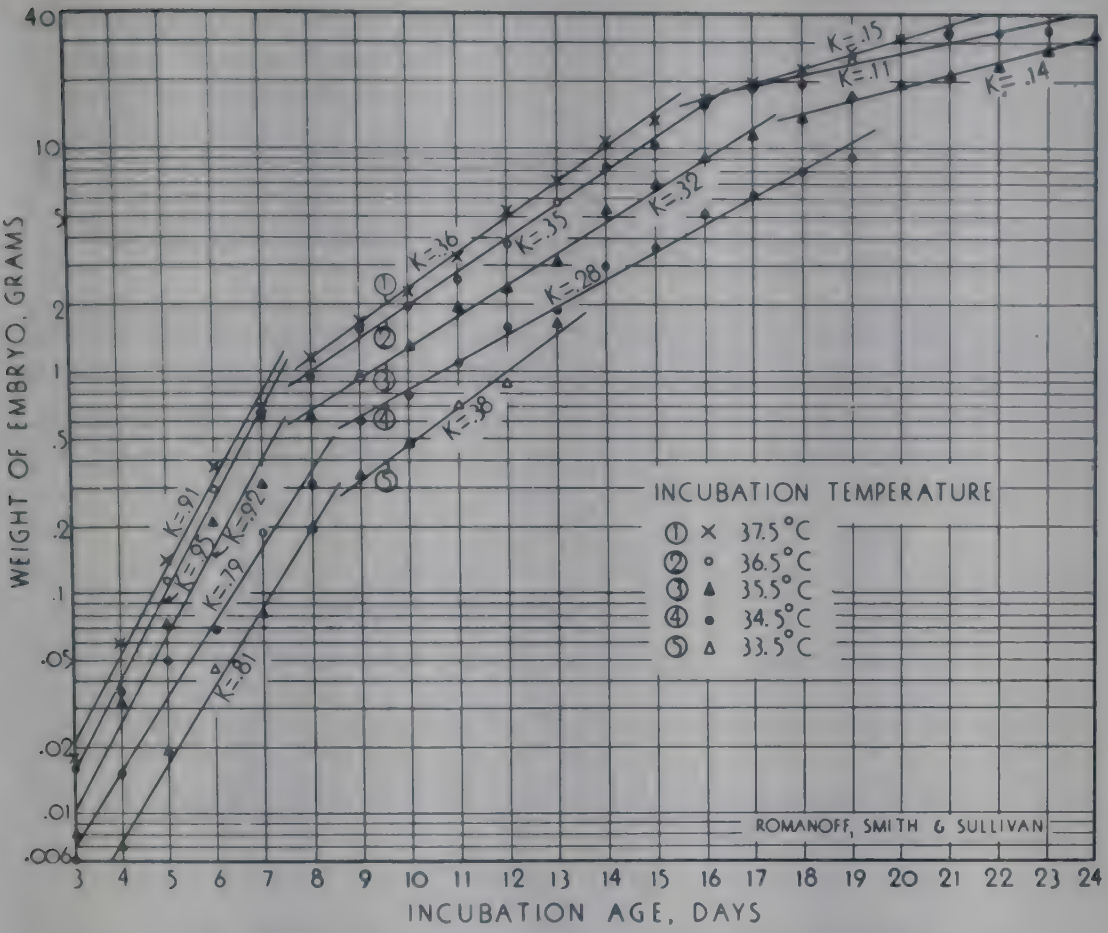

Fig. 11.2b. Same as in Fig. 11.2a, but based on Romanoff's data, which checks ours in Fig. 11.2a.

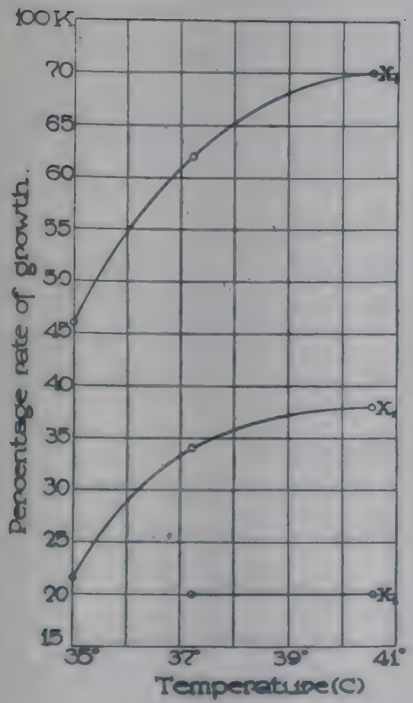

Fig. 11.3. The relation between the differential growth rate, k, and temperature for segments X_1, X_2, and X_3, of the growth curves in Fig. 11.2a.

cited. Prevost and Dumas[25] thought that incubation might be successful between 30° and 40° C; Daerste,[26] between 35° and 39° C. Pembrey and Gordon[27] suggested that in the earliest stages the chick embryo behaves like a cold-blooded animal; and they were also the first to observe that CO_2 production in chicks increases with environmental temperature. Recent contributions are those of Romanoff,[28] Barott,[29] Byerly,[30] and others.

Age changes in homeothermy during aging are discussed in Chapter 18.

11.5: Homeothermic mechanisms. The temperature of the living body, like that of an inanimate object, tends to come into heat equilibrium with the environmental temperature by conduction, convection, and radiation.

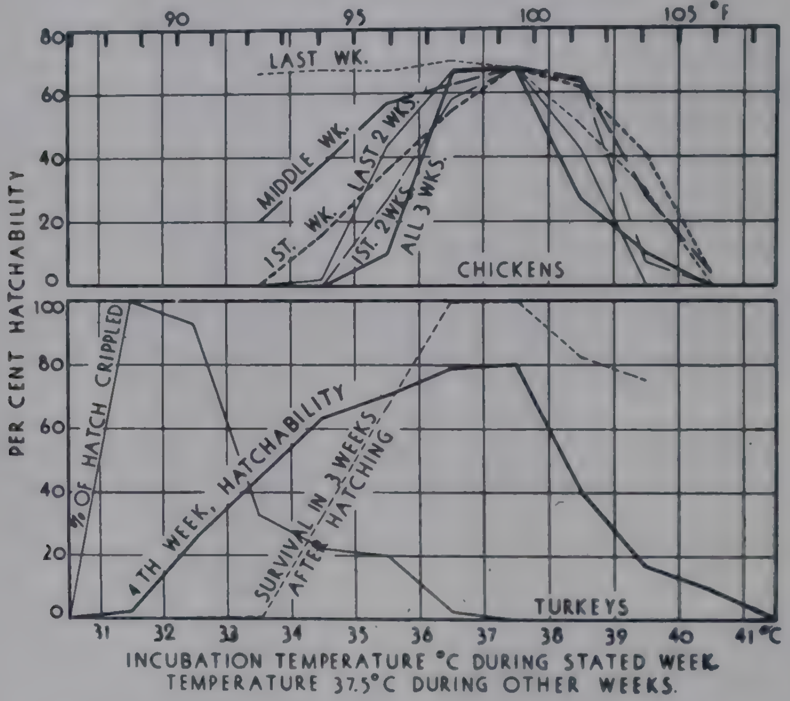

Fig. 11.4. Hatchability of chicken and turkey eggs at different temperatures. The optimum temperature is between 36.5 and 37.5° C, or about 97–100° F. Low temperature induces crippling.

Definitions: Heat *conduction* is a molecular-contact process. Metals *conduct* heat readily; wool, feathers, hair, fat, silk, wood, and air conduct heat poorly. Hence, we use a metal tea pot but wooden handle, and a "warm" woolen carpet (full of air pockets) on a "cold" metal or concrete floor. The rate of heat conduction is proportional to surface area and to temperature gradient.

Heat *convection* is by air movement, as by fanning.

Heat *radiation* is by electromagnetic waves at the rate of 186,000 miles per second, in straight lines, without physical contact of bodies. The electromagnetic spectrum includes waves ranging in length from cosmic rays, only 0.000,000,000,002 inch (or 0.000,000,01 micron), up through gamma rays, X-rays, (0.001 micron), ultraviolet rays (0.1 micron), visible light rays (V, B, G, Y, R), heat waves, Hertzian waves (.01 inch to 120 feet or 10,000 meters), radio waves (120 to 1220 feet), wireless telegraphy waves (1200 feet to 15 miles), and so on to hundreds of miles. Heat waves from the body are infrared waves, including only 5 to 20 μ (a μ is a micron, or a millionth of a meter, or a thousandth of a millimeter) in length ("Planck's law"). Heat loss by radiation depends, among other factors, on a surface quality called *emissivity*. Highly polished metals like copper or aluminum foil have a low emissivity of about 5 per cent as contrasted to 100 per cent emissivity of dead black material, 93 per cent emissivity of building materials (wood, paper, brick), 97 per cent emissivity of skin (white or "colored"). This means that if the temperature of the radiating body is higher than of the skin, the skin absorbs 97 per cent and reflects 3 per cent of radiated heat; the reverse occurs if the skin temperature is above that of the absorbing environment, absorption and emission being equal.

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[25] Prevost, J. L., et Dumas, J. B., *Ann. Sci. Nat.*, **4**, 47 (1825).

[26] Daerste, C., *Soc. Sci. Lille. Mem.*, Ser. **3**, 291 (1865).

[27] Pembrey, M. S., Gordon, M. H., and Warren, R., *J. Physiol.*, **16**, 5 (1894).

[28] Romanoff, A. L., Cornell Univ. Agr. Exp. Sta. Memoir, 132, 1930; *Id.*, Memoir, 150, 1933; *Id.* Bul., 616, 1934; *Id.* Bul., 687, 1938; *J. Agr. Sci.*, **25**, 318 (1935); *Poultry Sci.*, **15**, 311 (1936); *Anat. Rec.*, **65**, 59 (1936); *Science*, **94**, 218 (1941).

[29] Barott, H. G., "Temperature and energy metabolism of the chick embryo," U. S. Dept. Agr. Tech. Bull., 553, 1937.

[30] Byerly, T. C., "Incubation period," *Proc. Fifth World Congress*, **2**, 373 (1934) and other papers.

Several "laws" of radiation have been formulated, indicating that radiation is proportional to: temperature difference, surface area, and emissivity (Newton); surface area, emissivity, difference between the fourth powers of the absolute temperatures of the radiating body and the absorbing body (Stefan-Boltzmann); profile of projected area[31] (Lambert). Hardy[32] perfected methods for measuring heat radiation from the body.

It should be remembered in the following discussion that since the homeotherm must maintain its body temperature constant, its heat loss, or *thermolysis*, must equal its heat production, or *thermogenesis*. When the environment is hot, the problem is how to dissipate the body heat; when the environment is cold the problem is how to conserve the body heat and how to produce enough extra heat to keep the body temperature constant despite the unavoidable heat losses.

The loss or gain of heat by radiation, conduction, and convection is not a unique characteristic of living bodies, although it is only the living body that moves the blood to or from the surface for the best utilization of these mechanisms. The unique features of homeotherms are (1) conservation of body heat—reducing thermolysis—in cold weather by such means as developing fur, feathers, or subcutaneous fat, huddling as well as bundling ("social-temperature regulation") in some species, finding shelter, increasing heat production by muscular exercise or by increased production of thyroxine and/or adrenaline, reducing heat conductivity of skin by removing the blood from the surface, and reducing vaporization by decreasing respiration rate and by shutting off moisture production by the skin; (2) dissipation of body heat—increasing thermolysis—in hot weather by reversing the above processes, by reducing the skin covering, moving the blood to the surface for cooling, increasing vaporization rate by producing more surface moisture, sweat, by increasing the respiration rate, and by exposure to moving air (fanning).

[31] Bohnenkamp, H., *Pflüger's Arch. ges. Physiol.*, **228**, 40, 63, 79, 100, 125 (1931); and *Ergeb. Physiol.*, **34**, 84 (1932). This projected profile or "effective surface" is approximately 80 to 85 per cent of the anatomic surface area.

[32] Hardy, J. D., "Measuring radiation and surface temperature," *J. Clin. Inv.*, **13**, 593, 605, 615, and 817 (1934). Hardy, and Soderstrom, G. F., *Rev. Sci. Instruments*, **8**, 419 (1937). See also, Aldrich, L. B., *Smithsonian, Misc. coll.*, **81**, no. 6, 1928.

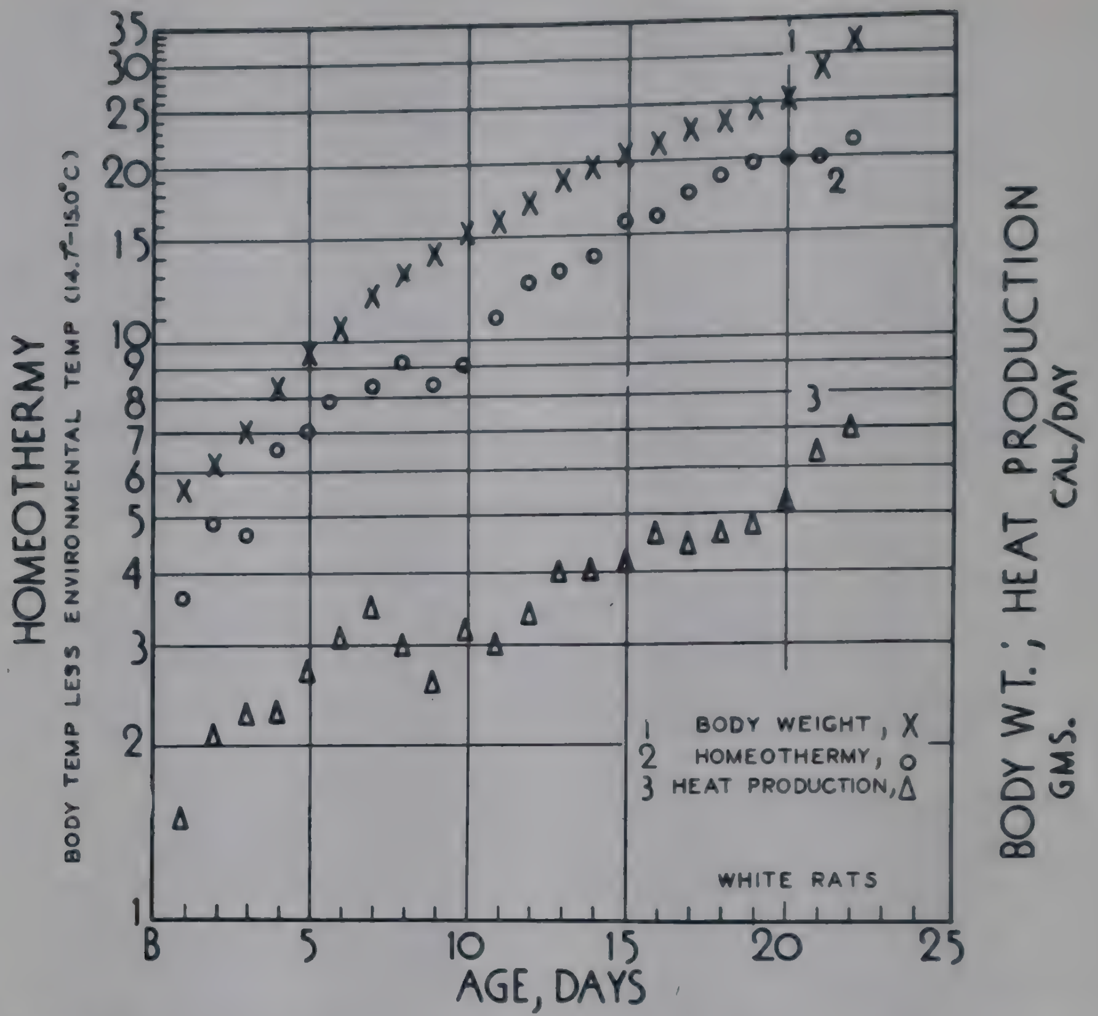

Fig. 11.5a. Age curves of development of homeothermy (curve 2), body weight (curve 1), and heat production (curve 3) in rats, with respect to an environmental temperature of approximately 15° C (59° F). Unpublished chart by E. B. Brody.

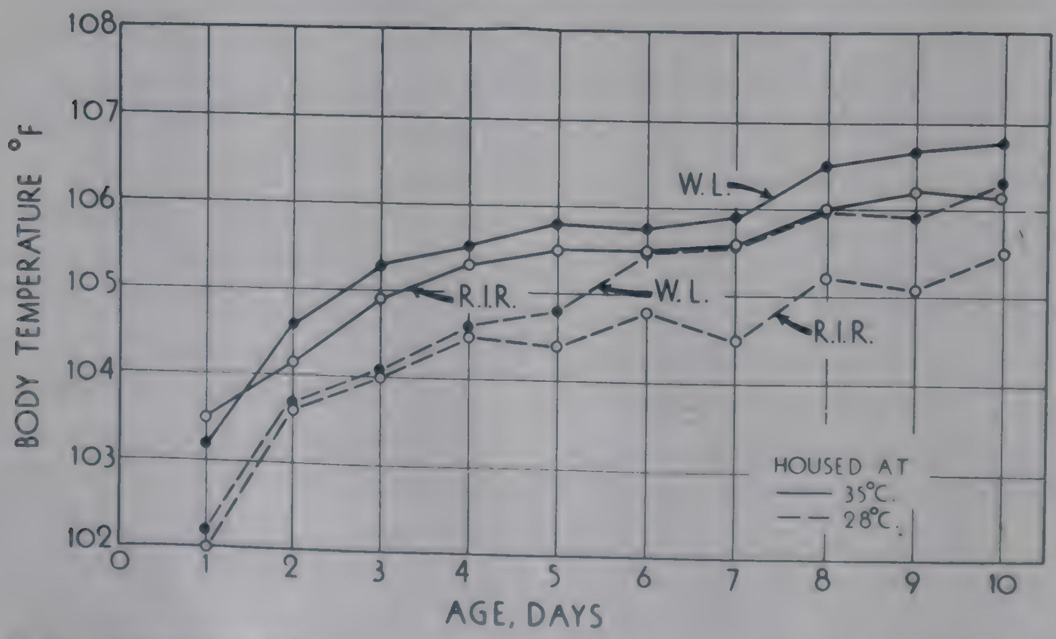

Fig. 11.5b. Age curves of body temperature in chicks brooded at 28° C and 35° C. The curves for the two temperatures tend to come together with increasing age, an index of homeothermic stabilization. From J. C. Scholes and F. B. Hutt, "Relation between body temperature and resistance to pullorum," Cornell Univ. Agr. Exp. Sta. Memoir 244, 1942.

Let us first inspect Figs. 11.6 to 11.9 indicating the influence of environmental temperature on heat dissipation by moisture vaporization.

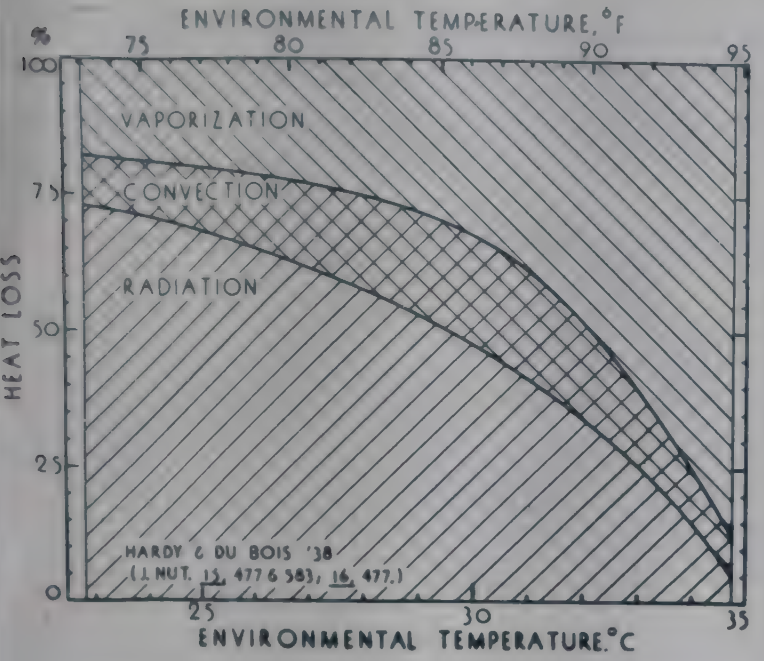

Fig. 11.6. Influence of environmental temperature on the percentages of heat loss by vaporization, convection, and radiation. Heat loss shifts from radiation to vaporization with rise in temperature.

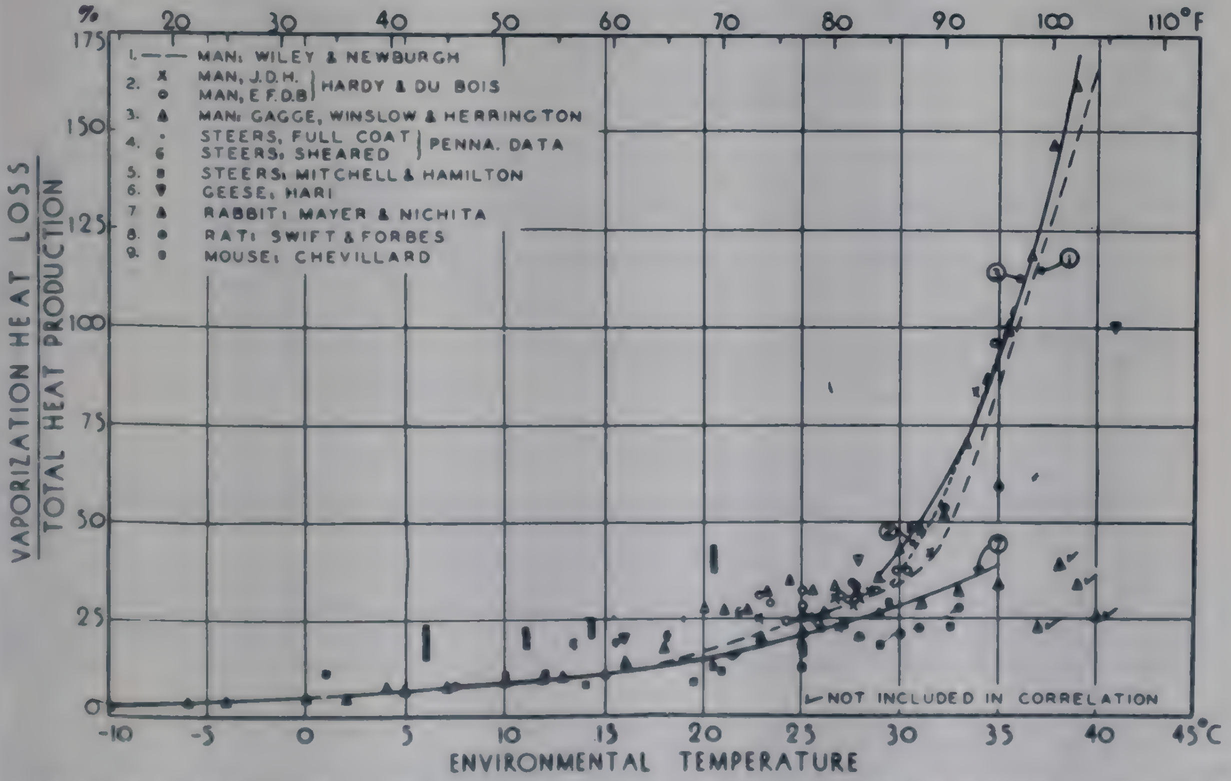

Fig. 11.7. Influence of environmental temperature on the ratio of heat dissipation by vaporization to the total heat production (or to the total heat dissipation) plotted on arithmetic paper. Note the break in the curves at about 85° F or 28° C.

It is obvious that if the environmental temperature is the same as that of the body, the body cannot lose heat by radiation, conduction, or convection; it must lose it all by vaporization. If the environmental temperature is higher than that of the body, the body absorbs heat from the environment—radiation, conduction, and convection are reversible processes—and the body must dissipate not only the heat *produced* by it but also that *absorbed* by it from the environment. This loss can be achieved by only one method, vaporization of moisture. Vaporization is a good cooling method because approximately 600 Calories or 2400 Btu of heat are dissipated for each quart, or liter, of moisture vaporization, and it is not unusual for a hard-working normal person to lose by vaporization in a hot, dry climate[33] three quarts per hour—over ten times the basal heat production or four times the heat production during hard physical labor.

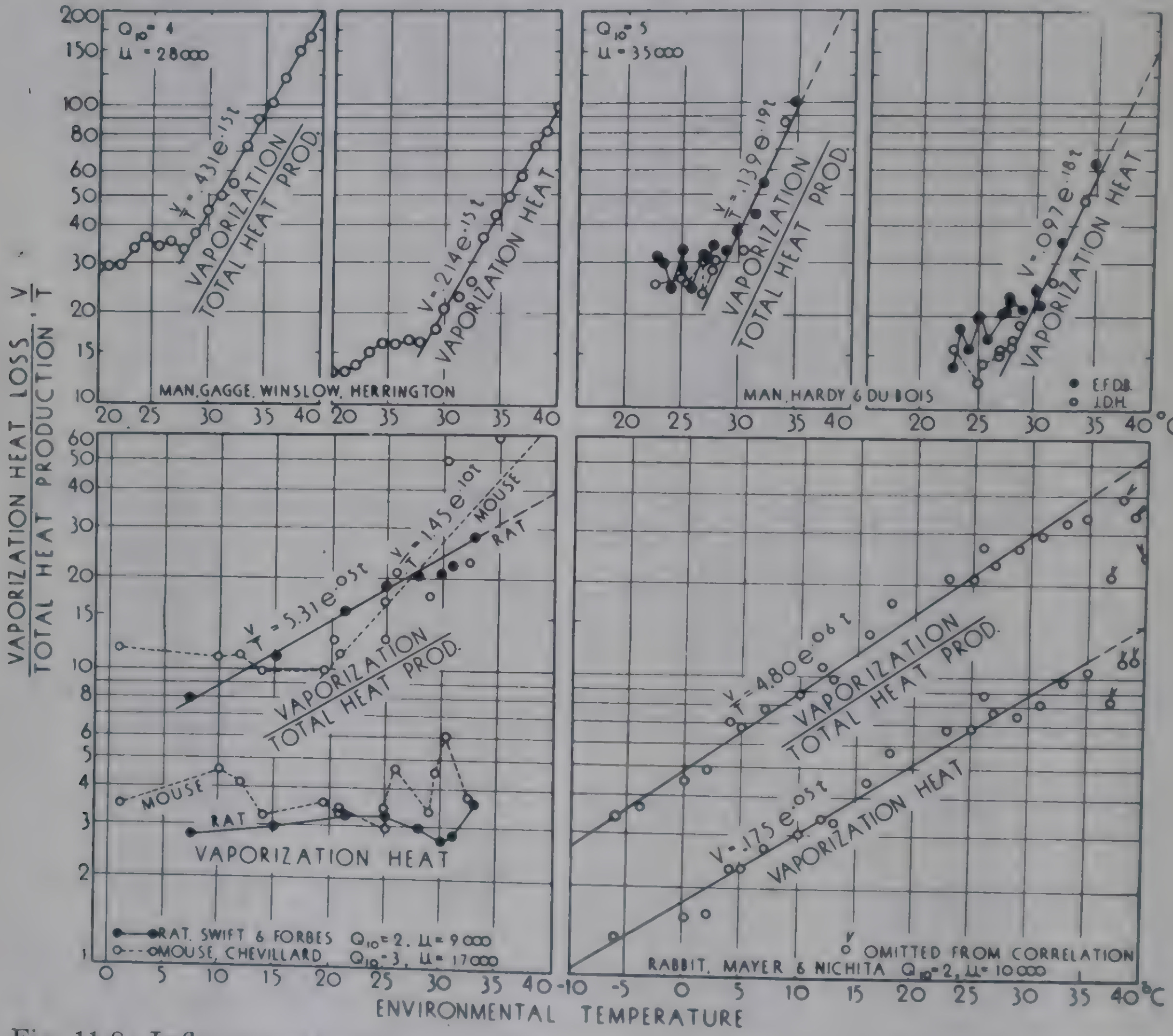

Fig. 11.8. Influence of environmental temperature on the ratio of heat dissipation by vaporization to the total heat production (or to the total heat dissipation) plotted on arithlog paper (the same data as in Fig. 11.7). Note the break in the curves at about 85° F or 28° C.

The importance of vaporization is brought into dramatic relief by considering the plight of unfortunate persons lacking sweat glands[34]. They are obliged to keep their underwear moist to enable them to bear normal summer temperature and they are unable to work because of rapidly rising body temperature on slight exertion.

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[33] Adolph, E. F., and Dill, D. B., "Water metabolism in the desert," *Am. J. Physiol.*, **123**, 369 and 486 (1938).

[34] Sunderman, F. W., *Arch. Int. Med.*, **67**, 709 (1941).

Fig. 11.6 shows that as the environmental temperature approaches body temperature, heat dissipation is shifted from radiation, conduction, and convection to vaporization. There is, however, a striking difference in this respect between the profusely sweating species, man, and the other species represented in Figs. 11.7 to 11.9 which are slightly or non-sweating.

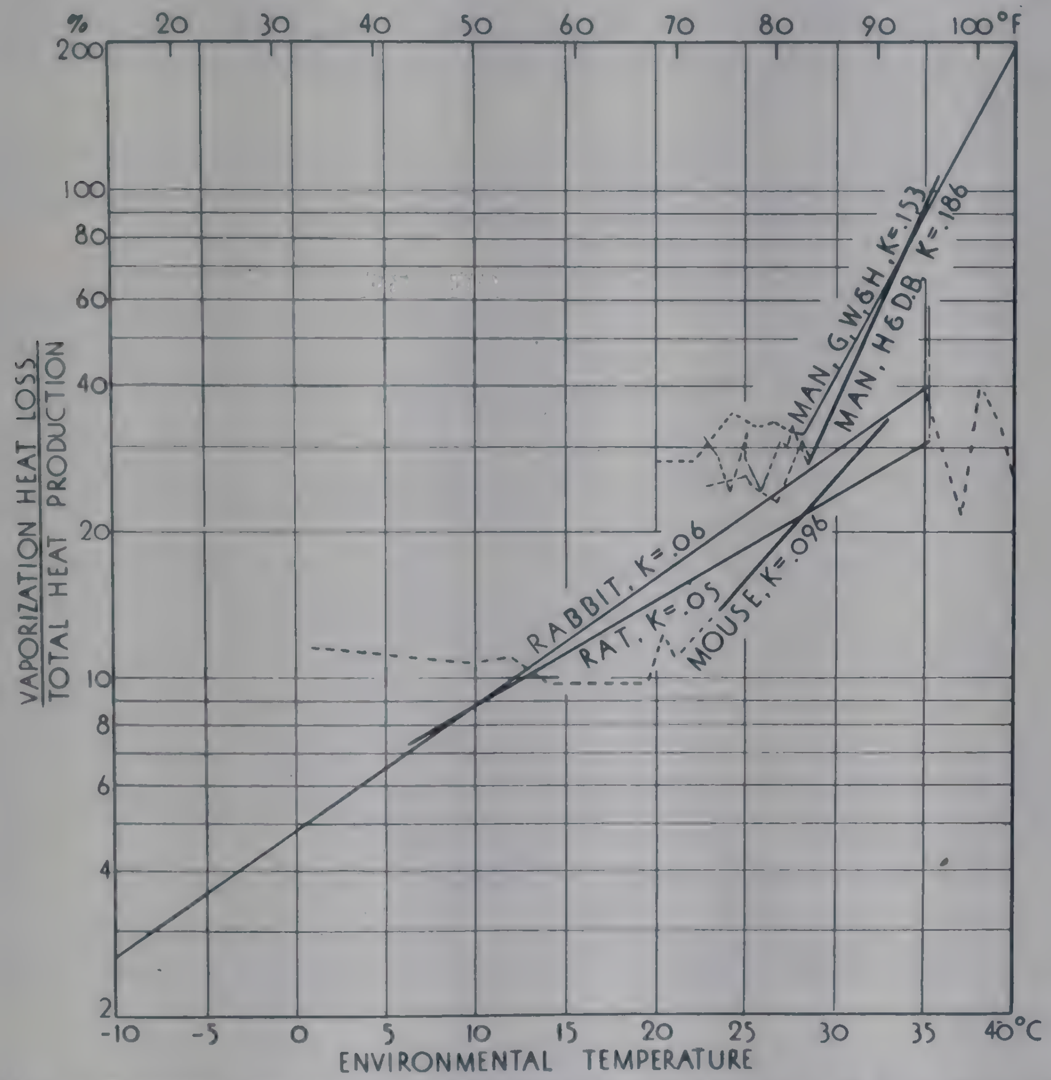

Fig. 11.9. Influence of environmental temperature on the ratio of heat dissipation by vaporization to the total heat production (or to the total heat dissipation) plotted on arithlog paper (the same data as in Fig. 11.7). Note the break in the curves at about 85° F or 28° C.

Figs. 11.7 to 11.9 show that there is a sharp break in the curve for man at temperature 29° C or 84° F (the "critical temperature" for sweating[35] in man is between 27° and 32° C). Up to this temperature vaporization increases irregularly, up to 35 per cent of the total heat dissipation; following this temperature, there is a very steep but orderly rise, a linear rise on the arithlog grid charts (Figs. 11.8 and 11.9), at the differential rate of 15 to 19 per cent per 10° C rise in environmental temperature, the Q_{10} being 4.5 to 4.9, or the u, 28,000 to 35,000. Thirty-five per cent of the heat production is dissipated by vaporization at 29° C (84° F), 100 per cent at 35°–36° C (95°–99° F), and 200 per cent at 40° C (104° F). In other words, at about 100° F all the thermolysis in man is by vaporization; and at 104° F the body absorbs as much heat from the environment as it produces, so that thermolysis by vaporization is twice the thermogenesis. When the inhaled temperature is 43° C (109° F), the exhaled air is 34° C (93° F): the air is cooled[33] by some 16° F in passing through the body.

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[35] Kuno, Y., "The physiology of human respiration," London, 1934.

The above discussion is for man, a profusely sweating species. The same holds true for the burro[33] (donkey or ass), which is also profusely sweating, and perhaps for the horse and mule.

The curve of heat dissipation with increasing environmental temperature is quite different in the slightly sweating or perhaps non-sweating species, which includes the other farm and laboratory animals: cattle, sheep, swine, rabbits, rats and mice, cats and dogs[36]. Figs. 11.7 to 11.9 show no break for these species at 29° or indeed at any other temperature. Their respiration rate goes up enormously, but this does not help the animal much above 35°C (95°F). The increase in percentage dissipation by vaporization rises slowly, about 10 per cent per 1° C rise in environmental temperature for mice and 5 to 6 per cent for the other species: the Q_{10} is 3.2 for mice and 1.7 for the other species; the u is 17,000 for mice and 10,000 for the other species. This plight of non-sweating species in hot weather is evidenced by the fact that under such conditions man dissipates only one-third of his heat by vaporization from the respiratory passages, two-thirds from the skin.

The respiration rate in man is relatively independent of temperature. There is some tendency toward a *lower* respiration rate in summer than in winter, but this is attributed[37] to seasonal differences in sunlight rather than temperature.

In cattle[38], on the other hand, as shown in Fig. 11.10—and this is true of other non-sweating species, such as sheep, swine, dogs, chickens[39]—the respiration rate *rises* rapidly with increasing environmental temperature to compensate for the inability to sweat, and to increase the vaporization rate from the respiratory passages.

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[36] For the contrasting reactions of dog and man to hot weather, see Dill, D. B., "Life, heat, and altitude," Harvard University Press, 1938. Dill, D. B., Edwards, H. T., Florkin, M., and Campbell, R. W., *J. Biol. Chem.*, **95**, 143 (1932). Dill, D. B., Bock, A. V., and Edwards, H. T., "Mechanisms for dissipating heat of man and dog," *Am. J. Physiol.*, **104**, 36 (1933).

[37] Lindhard, J., "The seasonal periodicity in respiration," *Skand. Arch. Physiol.*, **26**, 221 (1912).

[38] Kleiber, M., and Regan, W. M., "Influence of temperature on respiration of cows," *Proc. Soc. Exp. Biol. and Med.*, **33**, 10 (1935). Regan and Freeborn, S. B., "The effect of fly sprays on certain physiologic processes of the dairy cow," *J. Dairy Sci.*, **19**, 11 (1935). Regan, W. M., and Richardson, G. A., "Reactions of the dairy cow to changes in environmental temperature," *Id.*, **21**, 73 (1938). Rhoads, A. O., "Environmental temperature and respiratory rhythm of dairy cattle in the tropics," *J. Agr. Sci.*, **26**, 36 (1936). Kelley, M. A. R., and Rupel, I. W., "Stable environment and milk production," U. S. Dept. Agr. Tech. Bull., 591, 1937. Brody, S., "Reactions of animals to temperature, humidity, and air movement," *Proc. Am. Soc. Agr. Eng.*, St. Paul, (1939); *Agricultural Engineering*, **21**, 265 (1940); also in *Heating and Ventilating*, pp. 28-32, 1940. Brody, S., Chapter on "Temperature factors in animal production" pp. 462-473 in the book "Tem-

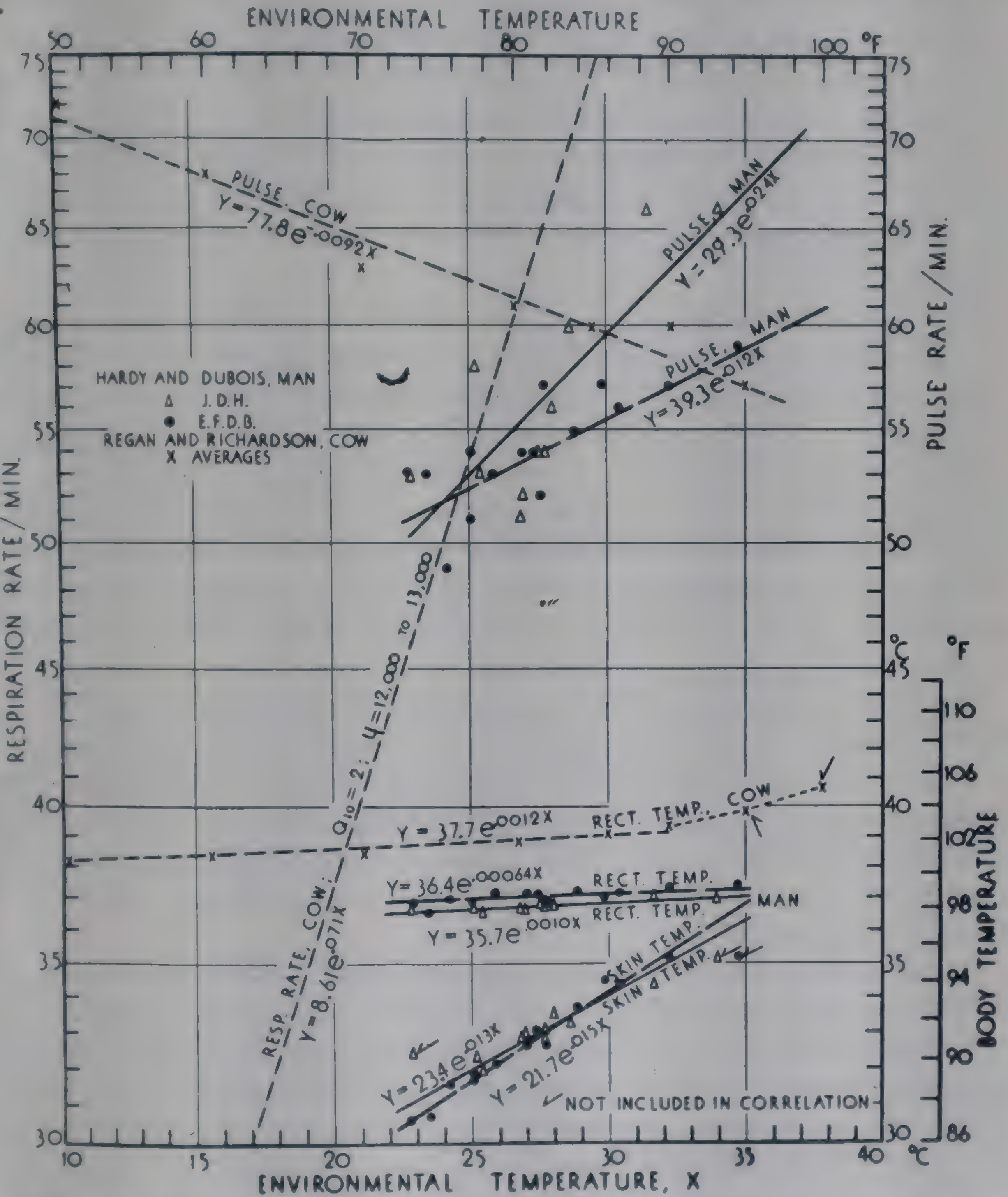

Fig. 11.10. Relative influence of rising environmental temperature on respiration rate, pulse rate, and rectal temperature in man and cow.

Fig. 11.10 indicates that in cattle the respiration rate is approximately

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perature, its Measurement and Control in Science and Industry," Reinhold Pub. Corp., 1941.

[39] Randall, W. C., and Hiestund, W. A., "Panting in chickens." *Am. J. Physiol.*, **127**, 761 (1939). Shelley, W. B., and Hemingway, A., "Thermal polypnea in dogs," *Id.*, **129**, 629 (1940).

doubled for an increase of 10° C (18° F) in the environmental temperature. According to the Van't Hoff law, the speed of a process is doubled for an increase in 10° C in the reacting system; but for the respiration rate it is doubled not for an increase in 10° C in the body, which is the reacting system, but in the environment. How shall one who accepts the Van't Hoff law explain this peculiar type of applicability? It may be that the temperature of the thermostatic trigger mechanism varies directly with the environmental temperature, even though the temperature of the body as a whole is not changed. The same explanation may be given for the increase in sweating rate in man (Figs. 11.7 to 11.9).

Fig. 11.10 also contrasts the effect of rising environmental temperature on the pulse rate of sweating and non-sweating species[38, 40]. In sweating species, the blood is shunted to the surface where it is cooled by the vaporization of sweat. The internal blood deficiency resulting therefrom is compensated by increased pulse rate. In non-sweating species, on the contrary, the pulse rate declines with increasing environmental temperature, presumably because in the absence of sweat the skin is not cooled. The blood may, therefore, be sent to the interior instead of to the surface, as in the case of sweating animals, and the overabundance of blood in the interior with its associated O_2 reservoir may depress the pulse rate.

The contrasting influence of a given high environmental temperature on the skin temperatures of sweating and non-sweating animals may be inferred from the relative dry- and wet-bulb thermometer readings. In Boulder City, Nevada, where a dry-bulb thermometer registered[33] 40° C and a wet-bulb thermometer read 22° C, the skin of a non-sweating animal probably "felt"[41] a temperature near 40° C (104° F) while that of a sweating animal "felt" a temperature nearer 22° C (72° F).

In cold weather the problem is, of course, to reduce heat loss by such devices as reducing vaporization (by cutting off sweating), reducing respiration rate, shunting the blood from the surface to the interior, huddling, and in the long swing, producing warm coverings of fur or feather and subcutaneous fat. The so-called chemical method of heat regulation consists of increasing thermogenesis by exercise, including shivering and muscle tension[42], increasing *SDA*

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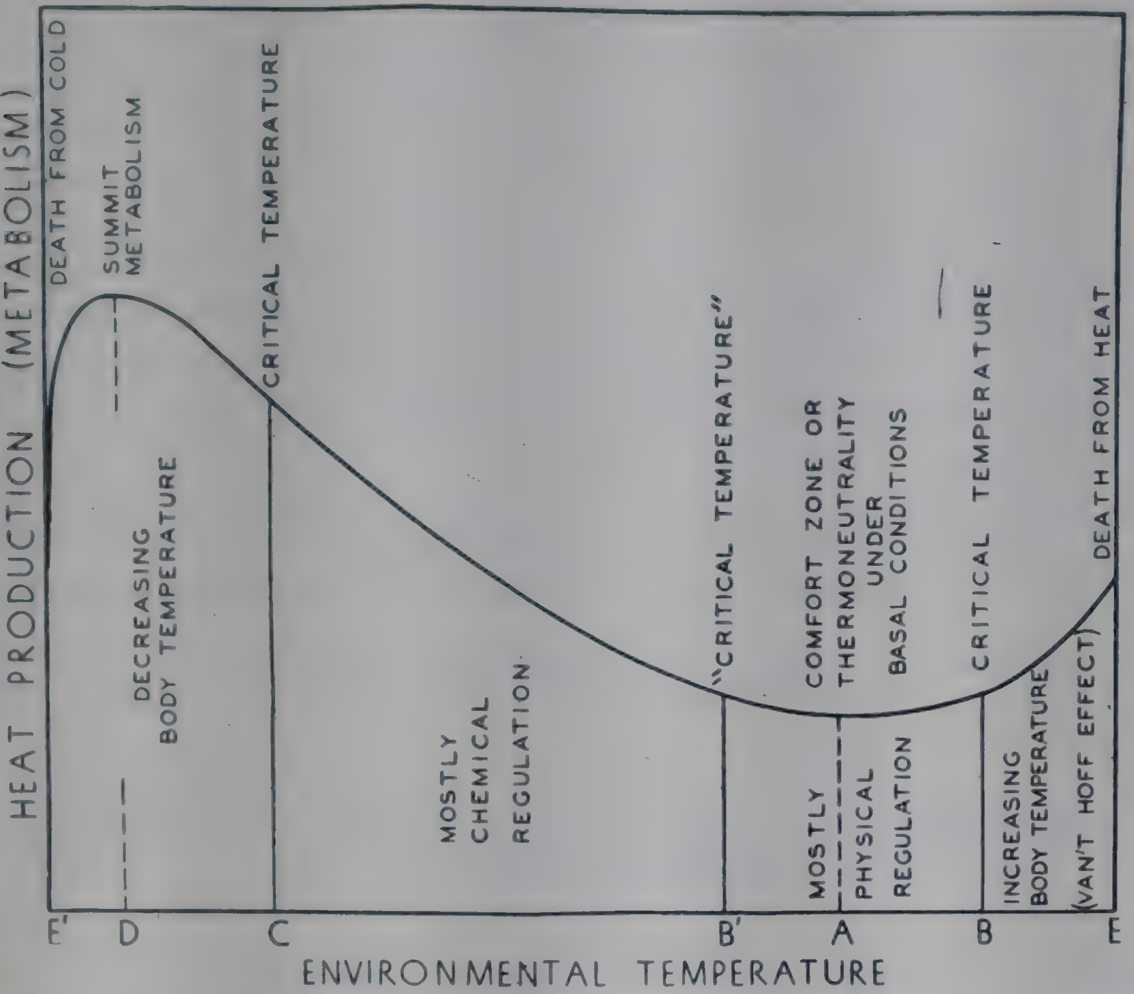
[40] Hardy, J. D., and DuBois, E. F., "Basal metabolism, radiation, convection, and vaporization at temperatures 22° to 35° C in man", *J. Nut.*, **15**, 481 (1938).

[41] The wet-bulb thermometer is an ordinary mercurial thermometer with the bulb tightly enclosed in a cloth, the lower end of the cloth extends beyond the bulb and deep into water. The vaporization from the wet cloth cools the wet bulb with resulting lower temperature. The *effective temperature* of the air-conditioning engineer is, indeed, estimated by comparing the temperature readings on the wet and dry-bulb thermometers.

[42] Swift, R. W., "Influence of shivering on heat production," *J. Nut.*, **5**, 227 (1932). (Shivering increases heat production 400%; it begins when skin temperature attains 19° C (66° F).)

by greater food intake (Ch. 4), and increasing adrenal and thyroid activity, adrenaline and thyroxine being powerful metabolic accelerators.


HEAT PRODUCTION (METABOLISM)
DEATH FROM COLD
SUMMIT METABOLISM
CRITICAL TEMPERATURE
DECREASING BODY TEMPERATURE
MOSTLY CHEMICAL REGULATION
"CRITICAL TEMPERATURE"
COMFORT ZONE OR THERMONEUTRALITY UNDER BASAL CONDITIONS
MOSTLY PHYSICAL REGULATION
CRITICAL TEMPERATURE
INCREASING BODY TEMPERATURE (VAN'T HOFF EFFECT)
DEATH FROM HEAT
E'
D
C
B'
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ENVIRONMENTAL TEMPERATURE

Fig. 11.11a. Diagram of the influence of environmental temperature on heat production and body temperature.

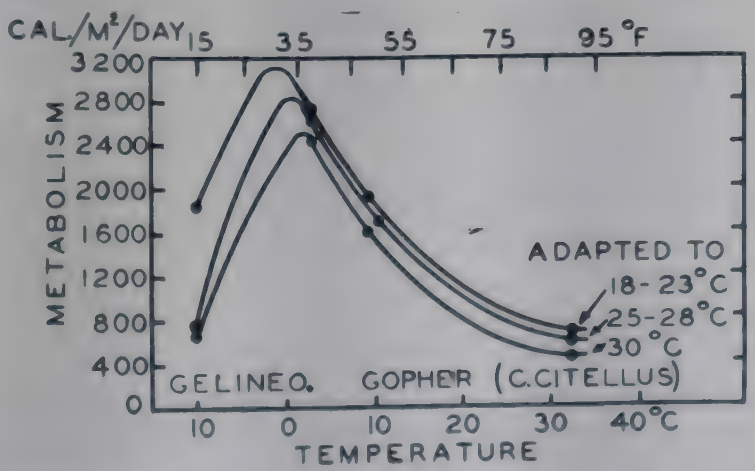

Fig. 11.11a. Illustrates Fig. 11.11 on a gopher or ground squirrel (a hibernating animal).

The relation between chemical and physical heat regulation is illustrated in Fig. 11.11, in which heat production is plotted against environmental temperature, modeled somewhat after Giaja[43]. Temperature segment *B-B′* includes the zone of thermoneutrality and also that of physical temperature regulation. At *thermoneutrality*[44], indicated by *A* in Fig. 11.11, the animal does not employ thermoregulatory devices: the environmental temperature is perfectly adjusted to keep the body temperature normal without regulation, and the animal feels neither hot nor cold. Thermoneutrality is presumably in the air-conditioning engineer's "comfort zone". The comfort zone for man is considered to be between 22° and 30° C or 72° to 85° F.

Thermogenesis begins to increase at environmental temperature *B′* in order to balance the increasing thermolysis. At environmental temperature *C* the body temperature begins to decline despite the increasing thermogenesis. The temperature-regulating mechanism is no longer able to cope with the cold.

Environmental temperature *D* in Fig. 11.11 represents the position at which heat production is maximum, the *summit metabolism* of Giaja[43]. Further decline in environmental temperature breaks down the homeothermic mechanism, and heat production as well as body temperature declines.

The following table, compiled from Giaja's papers, illustrates the levels of summit metabolism, metabolic quotient, and thermogenic reserve. These values vary with

Animal	Body weight (g)	Cal/sq meter		Metabolic quotient (summit/basal metabolism)	Lowest temperature, at which animal can maintain normal body temperature for 1 hr.	
		Basal metabolism	Summit metabolism		°C	°F
Swallow	19	1630	4830	3.0		
Mouse	18	1246	4350	3.4		
Dog	6375	1000	3500	3.5		
White rat	114	839	3058	3.6	−25	−13
Love bird	30	1764	6900	3.8		
Quail	97	1140	4658	3.8		
Sparrow	30	1274	5199	4.0	−30	−22
Finch	13	1534	6553	4.2	−30	−22
Duck	1950	1047	5177	4.9	−100	−148
Eagle	3450	635	4094	6.4		
Hedgehog	925	677	4521	6.6		
Goose					−90	−130
Pigeon					−85	−121
Fowl					−50	−58
Rabbit					−45	−49
Dove					−45	−49
Turkey					−40	−40
Guinea pig					−15	+5

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[43] Giaja, J., "La marge de thermogénèse et le quotient métabolique au cours du développement embryonnaire et de la croissance," *Ann. physiol. physico-chimie biol*, **1**, 596 (1925). "Homéothermie et thermorégulation," "Actualités scientifiques et industrielles," Nos. 576 and 577, Paris, (Herman et Cie, 6 rue de la Sorbonne), 1938. "Le métabolisme de sommet", *Réunion plénierè Sociétè de biologie* tenue less 17 et 18 *mai* (1929).

[44] Thermal neutrality, or thermal zero, is the environmental temperature at which heat loss from the body is equal to the *minimum* heat production. This thermoneutrality temperature is 7° to 10° C (12° to 18° F) below the rectal temperature and in man about 5° C (9° F) below the *average* skin temperature, although the temperature of the feet is nearly the same as of the environment at thermoneutrality.

species and size of the animal and with the temperature to which the animal is acclimatized[45]. Thus in rats the metabolic quotient[46] is 1.3 when it is acclimatized to 31° C, 2.8 to 18° C, 3.4 to 1° C.

The above table shows that the *thermogenic reserve*, or the thermal adaptability, is 2 to 3 times as great in the eagle as in the swallow. Immature animals have a smaller reserve than mature ones, and Giaja employed this metabolic reserve as an index of development of the heat-regulating mechanism in early growth. The homeothermic accommodation *range* (from temperatures *B* and *D* in Fig. 11.11) is 130° to 140° C in ducks and geese, 125° C in pigeons, 85° C in rabbits, 80° C in doves and larks, 70° to 90° C in fowl, 70° C in passerine birds (finches, sparrows, etc.) 65° C in rats, 55° C in guinea pigs.

On the right, high-temperature, end of the curve in Fig. 11.11, the body temperature begins to rise at environmental temperature *B*. The position of *B* varies with (1) sweating mechanism; (2) relative humidity and air motion; (3) nature of insulation (fur, feather, fat); (4) ratio of surface area to weight (a function of size, the larger the animal the smaller the surface per unit weight); (5) body temperature; (6) other factors, such as acclimatization. Figs. 11.11a and 11.12 illustrate the influence of acclimatization on gopher and rat respectively.[47] In the rat[48] the body temperature begins to rise at 32° C if acclimatized to −12° C, at 33° C if acclimatized to 12°–18° C, at 35° C if acclimatized to 29°–32° C.

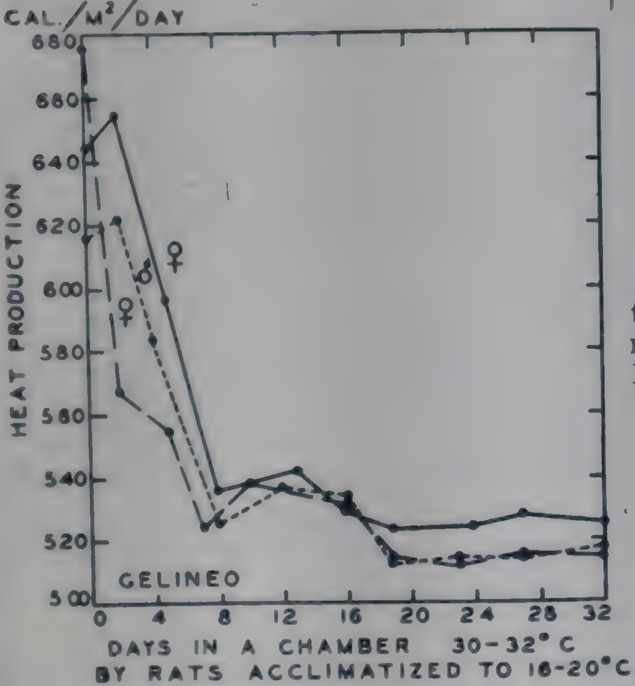

Fig. 11.12. The influence of acclimatization to a 30°–32° C environment on the metabolism of a rat previously housed in a 16°–20° C environment.

Herrington[49] reported that temperatures *B* and *B′*, the temperature limits of thermoneutrality, are 27–29° C (81–84° F) for rats, 28–30° C (82–87° F) for mice, 29–31° C (84–

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[45] Giaja, J., and Gelineo, S., "Sur la resistance au froid de quelques homeothermes," *Arch. intern. Physiol.*, **36**, 20 (1933).

[46] *Cf.* Gelineo, S., "Influence du milieu thermique d'adaptation sur la thermogenese des homeothermes," *Ann. Physiol. physicochim. biol.*, **10**, 1083 (1934).

[47] Gelineo, S.,[46] Schwabe, H. L., and Griffith, F. R., Jr., "The effect of prolonged exposure to low temperature on the basal metabolism of the rat," *J. Nut.*, **15**, 199 (1938).

[48] Gelineo, S.,[46] Ogle, C., and Mills, C. A., "Animal adaptation to environmental temperature conditions," *Am. J. Physiol.*, **103**, 606 (1933); **123**, 147 (1938). Bazett, H. C., *Am. J. Physiol.*, **123**, 197 (1938).

[49] Herrington, L. P., in the book "Temperature", etc., Am. Inst. Physics, Reinhold Pub. Corp., 1941.

88° F) for guinea pigs. However, Swift and Forbes[50] reported 30–33° C (86–91° F) for rats. The difference between Herrington and Swift's values for rats may be explained by differences in: speed of ventilation, humidity, and acclimatization. The temperature of thermoneutrality for women (nude) was reported to be[51] about 30° C (86° F). There are scattered references in the literature[52] on temperatures of thermoneutrality (with reference to heat production) of other species: 15–20° C (59–68° F) rabbit, 21–25° C (69–77° F) sheep, 13–21° C (55–70° F) goat, 20–26° C (68–78° F) dog, 20–29° C (68–84° F) chimpanzee, 18–25° C (65–77° F) goose, 20–28° C (68–82° F) turkey, 16–28° C (62–82° F) fowl, 24–25° C (75–77° F) pigeon, 31–36° C (87–96° F) dove, 34–36° C (93–97° F) canary, 30–31° C (86–88° F) finch. Lee[53] reported that thermoneutrality for the rabbit is 28° to 29° C (82–84° F).

It is instructive to note that the comfort zone of some poikilotherms on the farm is about the same as that of homeotherms. Thus, "Grasshoppers are forced to climb vegetation to escape heat which is at air temperature of about 80° F (27° C) and soil temperature of approximately 107° to 113° F (42° to 45° C)". "Maximum feeding is interrupted when air temperatures go much over 80° F, or soil temperatures above 113° F; the grasshoppers then climb vegetation, where most of them remain motionless only now and then nibbling on the vegetation on which they are resting."[54]

However, preceding this optimum temperature, the influence of environmental temperature on all metabolic processes of poikilotherms, including heat production, is directly opposite to its influence on homeotherms (Fig. 11.1). This temperature effect on insects is obviously very important, because it indicates that prior to the comfort zone the agricultural destructiveness of insects is increased 2 to 3 times for an increase of 10° C (or 18° F) in the environmental temperature.

Figs. 11.13 and 11.14 illustrate factually parts of the diagram in Fig. 11.11 and emphasize the following features: (1) other conditions being equal, the larger the animal, the flatter[55] its heat-production curve with decreasing environmental temperature; (2) if an animal is acclimatized to a low environmental temperature it produces more heat at higher temperatures than if it is acclimatized to the higher temperature (it takes time to change the thermostatic controls from one to another temperature level[56]); (3) the environmental-temperature range which animals can withstand on the cold side of thermoneutrality is very much greater than on the hot side.

Little is known about some of the homeothermic mechanisms, how, for example, fur or wool develops on approaching cold weather[57]; how more liquid fat develops on approach to winter and more solid fat on approach to summer[58].

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[50] Swift, R. W., and Forbes, R. M., *J. Nut.*, **18**, 307 (1939).

[51] Hardy, J. D., Milhorat, A. T., and Du Bois, E. F., "Basal metabolism and heat loss of young women at temperatures from 22° C to 35° C", *J. Nut.*, **21**, 383 (1941); also in the Book "Temperature", etc., Am. Inst. Physics, Reinhold Pub. Corp., 1941.

[52] *Cf.* Terroine, E. F., and Trautman, S., *Ann. Physiol. et physicochim. biol.*, **3**, 422 (1927); Giaja,[43] (1938).

[53] Lee, R. C., *J. Nut.*, **23**, 83 (1942).

[54] Parker, J. R., Univ. Montana Agr. Exp. Sta. Bull., 223 1930.

[55] Lapicque, L. et M., "Consommations alimentaires d'oiseaux de grandeurs diverses in fonction de la témperature exterieure," *C. R. Soc. Biol.*, **66**, 289, 67, 337 (1909). "Les echanges chez les homéothermes au repos en fonction de la grandeur corporelle et de la témperature exterieure", *Id.*, **66**, 528 (1909), and *C. R. Acad. Sci.*, **172** (1926).

[56] Ogle, C., and Mills, C. A.[57] Bazett, W. C., *et al.*, *Am. J. Physiol.*, **123**, 197 (1938). Mayer, A., and Nichita, G., *Ann. physiol. physicochim. biol.*, **5**, 609, 621 (1929). Gelineo[48].

[57] *Cf.* Mayer, A., Nichita, G., "Sur une adaptation du lapin aux temperatures élèvées, *Ann. physiol. physicochim. biol.*, **5**, 609, 621 (1929). Ogle, C., and Mills, C. A., "Animal adaptations to environmental temperature conditions," *Am. J. Physiol.*, **103**, 606 (1933); **107**, 635 (1934); **125**, 36 (1939).

As in homeostasy in general, so in homeothermy[59], the pioneering contribution to its mechanism was made by Claude Bernard about 1850. He cut a sympathetic nerve in the neck of a rabbit, resulting in dilatation of the blood vessels of the ear in engorgement with blood, and consequently increase in its

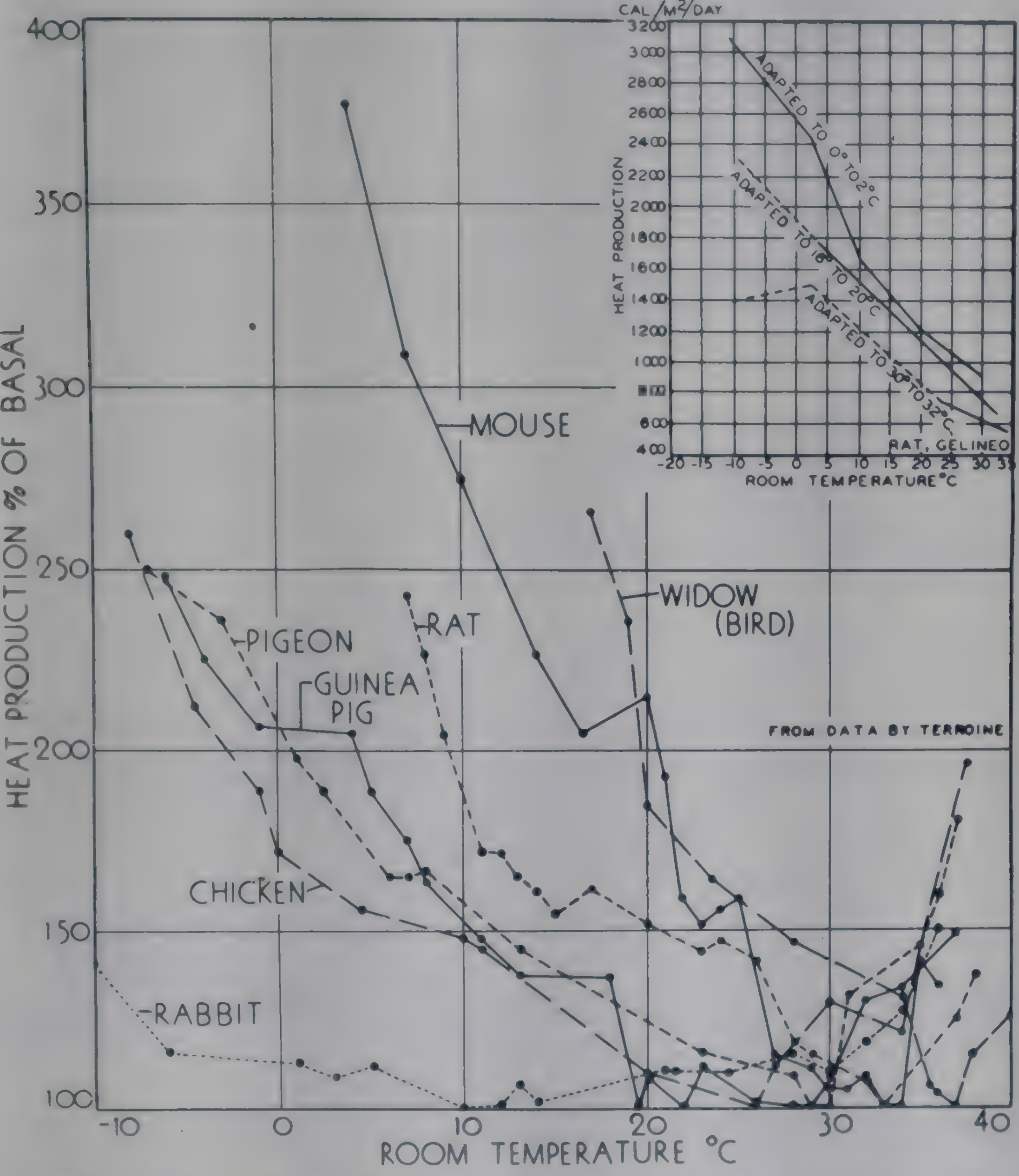

Fig. 11.13. Influence of environmental temperature on heat production of animals expressed as percentages of the minimum or basal heat production.

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[58] *Cf.* Henriques and Hansen, *Skand. Arch. Physiol.*, **11,** 151 (1901). Leathes and Raper, "The fats," London, 1925. Pearson and Raper, *Biochem. J.*, **21,** 875 (1927).

[59] Lusk, G., "The Science of Nutrition," Philadelphia, 1928; Du Bois, E. F., "Basal metabolism in health and disease," Philadelphia, 1936; Du Bois.[114] Cannon, W. B., "The wisdom of the body," 1932. Barbour, H. G., *Physiol. Rev.*, **2,** 295 (1921). Bazett, H. C., *Id.*, **7,** 531 (1927). Deighton, T., *Id.*, **13,** 427 (1933). Cannon, W. B., *Id.*, **9,** 397 (1929).

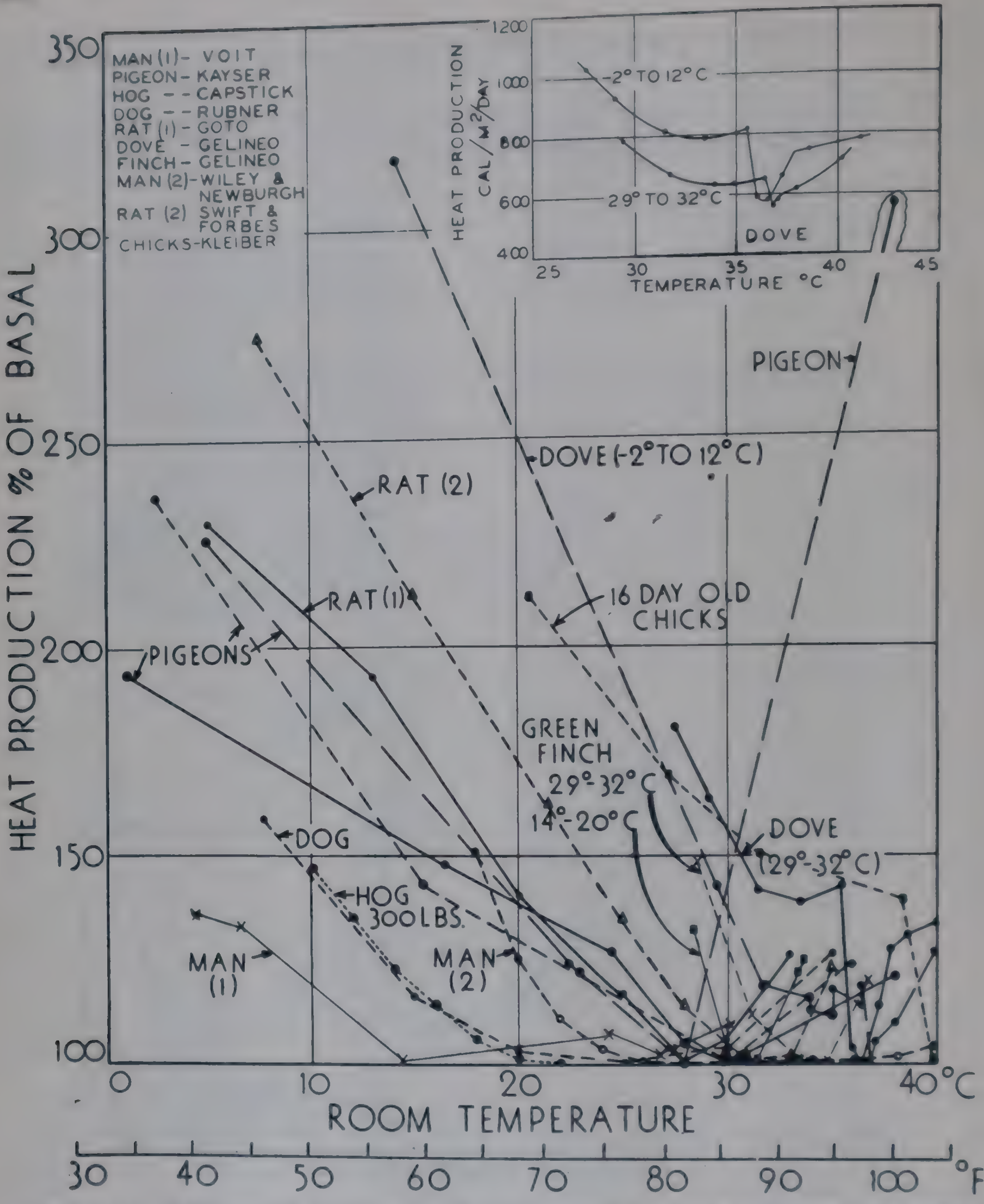

Fig. 11.14. Influence of environmental temperature on heat production of animals expressed as percentages of the minimum or basal heat production.

surface temperature[60]. It is now generally known that the sympathetic nervous system controls the caliber of many blood vessels and therefore, the conducting or insulating properties of the skin.

The nervous heat-regulating center is in the hypothalamus[61], at the head of the spinal cord, just below the cerebrum. In addition to the vasomotor con-

[60] Bernard, C., *Compt. Rend. Soc. Biol.*, **4**, 168 (1852).

[61] For review of his own important work and the literature, see Ranson, S. W., *Proc. Assn. Res. Nerv. and Ment. Dis.*, **20**, 342 (1940). See also Rogers, F. T., *Am. J. Physiol.*, **49**, 271 (1919); **66**, 453 (1923), and other papers.

trol of the caliber of the blood vessels and therefore flow and distribution of blood, the nervous system also controls the arrangement and position of hair or feathers—as in "ruffling" of feathers or "raising" of hair—so as to decrease or increase thermolysis. Incidentally, "goose flesh" in man is an obviously residual or surviving skin mechanism for arranging the fur which he lost. Tensing of muscles or shivering and other muscular activities associated with increasing heat production are under nervous control, directly or indirectly.

As an example of a possible indirect nervous control one thinks of the anterior pituitary which receives innervation from the hypothalamus, the heat-regulating center. Under hypothalamic influence, approaching cold may stimulate the pituitary to produce more thyrotropic[62] and adrenotropic hormones which stimulate thyroids and adrenals to produce more thyroxine (for slow, seasonal, temperature changes) and adrenaline[63] (for rapid temperature changes)[64].

Keeping rats in a cold environment for some time raises their basal metabolism even if measured at thermoneutrality (Figs. 11.12 to 11.15). This increase in heat production is attributed[65] to increased thyroid activity by cold. However, Lee and Lee[66] reported that the thyroid is not necessary for maintaining normal body temperature at low temperatures. Chahovitch[67] reported that thyroidectomy in the rat lowered "summit metabolism" from 17.6 to 9.3 Cal/kg/hr.

Chevillard, Hamon and Mayer[68] reported an increase in weight of the liver in mice kept in the cold. They[69] also reported the involvement of adrenal hormones and choline in heat regulation. Castration[70] appears to reduce the level of summit metabolism.

Bazett[71] reported that the blood volume of healthy men in Philadelphia is 15 to 40 per cent higher in summer than in winter; men exposed for a few days to high temperatures in midwinter experience an increase in blood volume, although not so striking as in summer. Cardiovascular changes were also observed.[72] The increase in blood volume must be related to the increase in the peripheral vascular bed. Bazett believes that the pituitary may be concerned in the changes of urine output occurring in the adaptation period.

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[62] Uotila, U. U., *Endocrinology*, **25**, 63 (1939).

[63] Cannon, W. B., Querido, A., Britton, S. W., and Bright, E. M., *Am. J. Physiol.*, **79**, 466 (1926–7). Cannon, "The wisdom of the body", 1932.

[64] For other references see: Cramer, W., "The thyroid-adrenal apparatus and its function in heat-regulation", *J. Physiol.*, **50**, p. XXXVIII (1915–16); **52**, 13 (1918); p. 36 (1915–16). Cramer, "Fever, heat regulation and the thyroid adrenal apparatus", London, 1928. Cannon, W. B., *et al.*, "Adrenal secretion in the chemical control of body temperature", *Am. J. Physiol.*, **79**, 466 (1926–27). Mills, C. A., "Effects of external temperature on thyroid activity", *Id.*, **45**, 557 (1917–18). Landauer, W., "Thyroid activity and environmental temperature in frizzle fowl", *Arch. Inter. de pharmacodyn. Ther.*, **49**, 125 (1934). Benedict, F. G., Landauer and Fox, E. L., "Metabolism, etc. in the frizzle fowl", Storrs Agr. Exp. Station. Bull., 177, 1932. Korenchevsky, V. "Influence of removal of thyroid, etc. on body temperature regulation," *J Path. and Bact.*, **29** (1926). Schmidt, L. H., and I. G., "Environmental temperature and thyroxin", *Endocrinology*, **23**, 535 (1938). Bodansky, M., "Temperature and the thyroid," *J. Exp. Med.*, **63**, 523 (1936).

[65] Schwabe, E. K., and Emergy, F. E., *Anat. Rec.*, **67**, Supp. 3, 46 (1937); Schwabe, Emergy, and Griffith, F. R., Jr., *J. Nut.*, **15**, 199 (1938). See also Ogle and Mills[57].

[66] Lee, M., and Lee, R. C., "Thyroidectomy, thyroid feeding and basal metabolism at different temperatures", *Endocrinology*, **21**, 790 (1937).

[67] Chahovitch, X., *Compt. Rend. Soc. biol.*, **100**, 1220 (1929).

[68] Chevillard, L., Hamon, F., and Mayer, A., *Ann. Physiol. Physicochim. biol.*, **13**, 493 (1937).

[69] Gasnier, A., and Mayer, A., *Ann. physiol. physicochim. biol.*, **13**, 620 (1937).

[70] Chahovitch, X., and Vichnjitch, M., *C. R. Soc. biol.*, **98**, 1153 (1928).

[71] Bazett, H. C., Proc. XVI. *Intern. Physiol. Congr. Zurich*, **2**, 76 (1938). Sunderman, F. W. Scott, J. C., and Bazett, *Am. J. Physiol.*, **123**, 199 (1938).

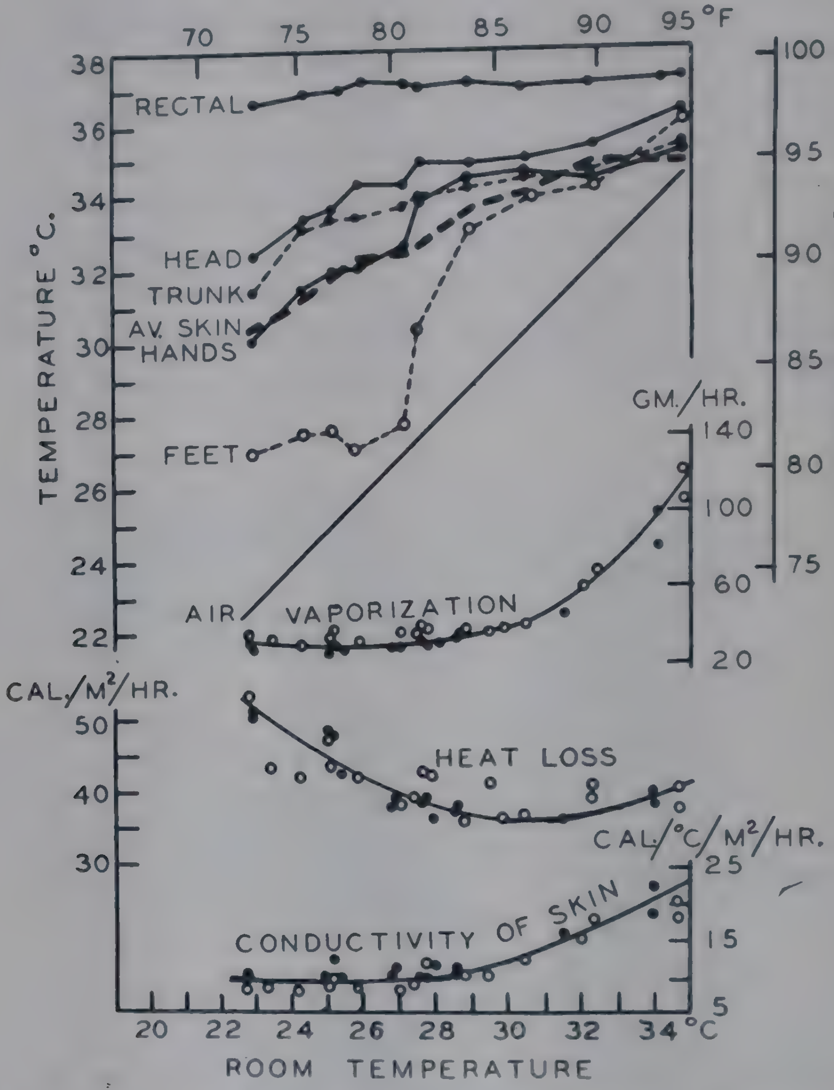

Fig. 11.15. A comparison of the influence of environmental temperature on metabolism, and on the temperature of several body regions, heat loss, and skin conductivity for heat. Modified from Hardy and Du Bois (see text).

11.6: Applications. The facts and principles of homeothermy may be utilized in calorimetry, animal husbandry, air-conditioning engineering, and medicine.

11.6.1: Insensible-perspiration calorimetry. In 1614 Sanctorious wrote a book in which he gave much attention to "perspiratio insensibilis", and decorated it with an engraving of a man suspended from a steel-yard scale watching himself losing weight—a rather fascinating pastime. This weight loss does not include liquids or solids, which are "sensible"; it includes only "insensible" losses, *e.g.*, water vapor and carbon dioxide. However, when the R.Q. is

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[72] Bazett, Scott, and Sunderman, *Am. J. Physiol.*, **123,** 11 (1938).

0.727, the CO_2 weight exhaled just balances the O_2 weight consumed[73] so that all "insensible" loss is vaporized moisture alone. The heat dissipated is computed by multiplying the weight of water vaporized by the latent heat of vaporization of the water (0.58, in the body nearer 0.60 Cal/gm water). Benedict and Root and others suggested that the heat production may be determined from insensible perspiration, since the heat dissipated by vaporization is an approximately constant percentage of the total heat produced or dissipated under a *given set of conditions* (Figs. 11.7–11.9), that is, below the sweating temperature of about 27° C (in man).

From Figs. 11.7 and 11.8 it is evident that this method is not applicable with precision following temperatures of 27° or 30° C, and that even prior to this temperature the percentage heat loss by vaporization is very sensitive to environmental temperature and other conditions. It increases from about 18 per cent of the total heat dissipation at 18°C (65° F) to about 35 per cent at 30° C (85° F), then very steeply to 100 per cent at 36° C (97° F), and so on.

As previously noted, in man (sweating species), about $\frac{2}{3}$ of the insensible moisture loss is from the skin, and $\frac{1}{3}$ from the respiratory passage[74]. In non-sweating animals, the moisture loss from the skin is less, only that which reaches the surface by "osmosis" or "physical permeability" rather than by glandular (sweating) activity. It has not been determined how environmental temperature affects the ratio of "osmotic" moisture[75] to sweat-moisture vaporization in sweating and (relatively) non-sweating species.

Incidentally, it should be possible to compute from the ventilation rate, that is, from the volume of air exhaled per unit time, the moisture vaporized from the respiratory passages, since the exhaled air is practically saturated with

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[73] The molar weight of O_2 is 0.727 of the molar weight of CO_2: $\frac{O_2}{CO_2} = \frac{32}{44} = 0.727$; hence, when the R.Q. is 0.727 the CO_2 exhaled just balances the O_2 absorbed. When the R.Q. is less than 0.727, more O_2 is absorbed than CO_2 exhaled, and the insensible water loss is greater than the total insensible loss; when the R.Q. is greater than 0.727 more CO_2 is given off than O_2 is taken in and the insensible water loss is less than the total insensible loss. The production of methane would, of course, complicate the situation. The insensible perspiration, I. P., may, therefore, be defined symbolically by the equation

$$\text{I.P.} = H_2O + (CO_2 - O_2)$$

or the moisture (H_2O) vaporized, by the equation

$$H_2O = \text{I.P.} - (CO_2 - O_2)$$

in which CO_2 and O_2 represent the weights of CO_2 produced and O_2 consumed. The value of $(CO_2 - O_2)$ is slight in any case, and zero when the R.Q. is 0.727.

[74] Richardson, H. B., "The effect of the absence of sweat glands on the elimination of water from the skin and lungs," *J. Biol. Chem.*, **67**, 397 (1926). F. C. Houghten, *Am. J. Physiol.*, **88**, 386 (1929), estimates that at 70° F (21° C) 25% of the heat is lost by vaporization: 16 per cent by vaporization from the skin and 9 per cent from the lungs; 50 per cent by radiation and 25 per cent by convection.

[75] Hancock, W., and Haldane, J. J., "The osmotic passage of water and gases through the human skin," *Proc. Roy. Soc.* **111B**, 412 (1932). Hancock, W., *et al.*, "The loss of water and salt through the skin", *Id.*, **105B**, 43 (1930). For influence of temperature on insensible perspiration in man, see also Kuno[35]; Adolph, E. F., *Am. J. Physiol.*, **66**, 445 (1923); Campbell, J. A., and Angus, T. C., *J. Ind. Hyg.*, **10**, 331 (1928); Houghten[74].

moisture at an almost constant temperature. Thus, assuming that the temperature of expired air in cattle is 38° C, and that it has a water vapor pressure of 49.8 mm Hg, the expired air contains $49.8/760 \times 100 = 6.6$ per cent water.

As noted, Benedict and Root[76] suggested using the insensible perspiration method for estimating heat production. Newburgh[77] perfected the method for long periods of observation on man, and Levine[78] and associates on infants.

In regard to farm animals, Lefèvre and Auguet[79] reported that the heat loss by vaporization in sheep increases with increasing environmental temperature.

Mitchell and Hamilton[80] reported that in steers the heat loss by vaporization ranged from about 15 per cent of the total heat loss at 43° F, to about 42 per cent at 69° F, (Fig. 11.7) and that following shearing the insensible loss decreased by from 5 to 30 per cent (average 20 per cent). The insensible loss was also influenced directly by the amount of water consumed (the skin is a water-storage organ, Ch. 10) and inversely by dehydration, and also by the individuality of the animal.

In connection with the influence of shearing on heat loss by vaporization, it is instructive to note that, although under given conditions normally feathered fowl lost 49 per cent of their heat by vaporization, scantily-feathered frizzle fowl lost only 17 per cent of their heat by vaporization[81] (because the normally-feathered bird loses little by radiation).

Mitchell and Hamilton's results substantiate those of Benedict and Ritzman[82], Kriss[83], Mayer, Lefèvre, Kayser[84], and others, namely, that heat dissipation as latent heat of vaporization varies with temperature and other factors (Fig. 11.7). Consequently, with the exception of very special conditions, insensible perspiration calorimetry is not the best method of measuring heat production or energy metabolism.

11.6.2: Partitional calorimetry. The evaluation of heat dissipation from insensible perspiration alone is somewhat crude. The heat produced by the body may be evaluated more precisely from four measurements: (1) vaporization, (2) infrared (heat) radiation, (3) conduction and convection, and (4) change of heat storage in the body. Winslow and associates[85] are attempting to develop a method, which they call *partition calorimetry*, and which they claim to be superior to the conventional direct or indirect calorimetry because (1) it indicates the manner in which the heat is lost; (2) it has no time lag to mask transitory and adaptive phenomena; (3) by proper adjustment of temperature and of radiating walls of the enclosure, radiation, convection, and vaporization may be varied independently and their interrelations investigated.

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[76] Benedict, F. G., and Root, H. F., "Insensible perspiration", *Arch. Int. Med.*, **38**, 1 (1926); Benedict and Wardlow, H. S. H., *Id.*, **49**, 101 (1932).

[77] Newburgh, L. H., *et al.*, "Total heat eliminated by the human being," *J. Clin. Inv.*, **8**, 147 (1930); "The relationship between the environment and the basal insensible loss of weight", *Id.*, **10**, 689 (1930); "A method for the determination of heat production over long periods of time", *Id.*, **10**, 703 (1931); "The exchange of energy between man and environment", Baltimore, 1930.

[78] Levine, S. Z., *et al.*, *Am. J. Dis. Children*, **33**, 204 (1927); **37**, 791 (1929); **39**, 917 (1930); **40**, 269 (1930); **44**, 732 (1932).

[79] Lefèvre, J., et Auguet, A., *C. R. Acad. Sci.*, **190**, 326 (1930). Lefèvre et Auguet, "Laboratoire de Bioenergetique," *Bull. Soc. Sci. Hyg. Alim.*, **18**, 328 (1930).

[80] Mitchell, H. H., and Hamilton, T. S., "Heat production of cattle from the insensible weight loss," *J. Agr. Res.*, **52**, 837 (1936). For vaporization in poultry, see Mitchell and Kelley, M. A. R., *J. Agr. Res.*, **47**, 735 (1933).

[81] Benedict, F. G., Landauer, W., and Fox, E. L., Conn. Agr. Exp. Sta. Bull , 177, 1932.

[82] Benedict, F. G., and Ritzman, E. G., "The metabolism of the fasting steer," Carnegie Inst. Washington Publ., 377, 1927.

[83] Kriss, M., "The insensible loss in body weight of cattle," *J. Agr. Res.*, **40**, 27, 283 (1930).

[84] Kayser, C., "L'émission d'eau et la rapport H_2O: O_2 chez quelque éspèces homeothermes adultes et en cours de croissance," *Ann. physiol. physiochim. biol.*, **6**, 721 (1930).

Partition calorimetry involves correction for changes in body temperature. Burton[86] estimates the average body temperature by the following relation:

$$\begin{array}{c}\text{Average body}\\ \text{temperature}\end{array} = 0.65 \times \text{rectal temp.} + 0.35 \text{ average surface temperature}$$

Incidentally, there is a temperature gradient[87] of 4° to 5° C between the body interior and the body surface, and Burton[88] estimates the conductance of heat from the interior to the surface by the relation:

$$\text{Conductance} = \frac{\text{rate heat loss from surface}}{\text{surface area} \times (\text{rectal less skin temperature})}$$

The so-called body temperature is a "spot temperature" and various parts of the body, especially different regions of the skin, vary enormously in temperature,[89] as illustrated in Fig. 11.15. When the room temperature is about 22° C, the rectal temperature in man is about 37° C, abdomen 35°–36° C, feet 27° C, and so on. The rectal temperature is least sensitive to changes in environmental temperature, the toes most sensitive, and so on.

The rate of heat loss from the nude body depends primarily on the peripheral circulation, but is modified by the amount of subcutaneous fat (the insulating value of fat is 3 times that of water). The greatest vasomotor changes are in the extremities, especially in the fingers and toes (less in hands, still less in forearms);[90] hence the hands and feet are among the most effective temperature regulators (heat radiators). About 30 per cent of the total vaporization comes from the hands and feet, although their surface area is only 12 per cent of the total body surface.[91] The ability to withstand rapid changes in environmental temperature depends on the rapidity of response of blood flow from or to the body interior, and especially to the extremities.

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[85] Winslow, C-E. A., Herrington, L. P., and Gagge, A. P., "Partitional calorimetry," *Am. J. Physiol.*, **116**, 641, 656, 669 (1936); **120**, 1, 277, 288 (1937).

[86] Burton, A. C., *J. Nut.*, **9**, 261 (1935).

[87] Bazett, H. C., and McGlone, B., "Temperature gradients in the tissues of man," *Am. J. Physiol.*, **82**, 415 (1927).

[88] Burton, A. C., *J. Nut.*, **9**, 261 (1935); *Ann. Rev. Physiol.*, **1**, 109 (1939).

[89] Benedict, F. G., and Slack, E. P., "Temperature fluctuations in different parts of the human body," Carnegie Inst Washington, Publ. 155, 1910. Murlin, J. R., *Ergeb. der Physiologie*, **42**, 153 (1939). Hardy and Du Bois[40, 51].

[90] Grant, R. T., Bland, E. F., and Camp, P. D., "Vascular reactions in the rabbits' ear with respect to cold," *Heart*, **26**, 69 (1932); Morton, J. J., and Scott, W. J. M., "Sympathetic vasconstrictor activity in the lower extremities," *J. Clin. Inv.*, **9**, 235 (1930); Pickering, G. W., "The vasomotor regulation of heat loss from the human skin in response to external temperature," *Heart*, **16**, 115 (1932).

[91] Benedict, F. G., and Wardlow, H. S. H., *Arch. Int. Med.*, **49**, 1019 (1932).

Incidentally, emotional breaking into "cold sweat" and "cold hands", especially cold fingertips, often associated with blushing, indicates suggestive interrelations in the central nervous system, the brain.[92]

11.6.3: Effect of cold weather on productivity and efficiency. It is generally known that farm livestock are wintered without apparent injury on the open range in severe winter weather. For instance, the winter temperature at Miles City, Montana, is frequently −40° F (−40° C) yet horses, cattle, and sheep in the government experiment station there are wintered outdoors without injury. In 1907 Waters,[93] at the Missouri Station, reported that beef cattle did better wintered outdoors than when conventionally housed. Dice[94] reported that dairy cattle wintered outdoors (9° to 27° F or −13° to −3° C) produced as well as when conventionally housed, and the feed cost of maintenance was not increased by the lower outdoor temperature.

Jordan[95] reported that dairy cows produced from 55 to 85 per cent more heat than was needed for maintenance of body temperature, and Armsby,[96] therefore, saw no reason why a cow "might not be subjected to comparatively low temperatures without causing any increased katabolism for the sake of heat production solely".

These results are not surprising because animals wintering outdoors respond to approaching cold weather by developing highly insulating coats of fur,[97] feathers, and subcutaneous fat. By driving the blood from the surface on declining temperature, the blood is kept from cooling and the skin becomes highly non-conductive to heat (Fig. 11.15). Moreover, incidental to their productive or even mainteinance processes, farm animals consume large quantities of feed associated with high heat production (Ch. 4), thus keeping the animal warm in cold weather, and making it unnecessary for the body to increase the oxidation of its tissues for maintaining normal body temperature. The rapid rise in *basal* (that is, fasting and resting) metabolism with declining environmental temperature is no indication that there is a similar rise in normally fed animals under farm conditions.

It is true that under basal-metabolism conditions the "critical" temperature (Figs. 11.11, 11.13, 11.14) of farm animals is 60° to 70° F (15 to 21° C). Such values were reported for domestic fowl[98], pigs[99], and steers[100].

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[92] List, C. F., and Peet, M. M., *Arch. Neurol. Psychiat.*, **39**, 1228 (1938); **40**, 27 (1938). For other references on related problems, see Sheard, Du Bois, and others in "Temperature", etc. Reinhold Pub. Corp., 1941.

[93] Waters, H. J., "Fattening cattle for market", Univ. Missouri Agr. Exp. Sta. Bull., 76, 1907.

[94] Dice, J. R., "The influence of stable temperature on the production and feed requirements of dairy cows," *J. Dairy Sci.*, **23**, 61 (1940).

[95] Jordan, W. H., "The feeding of animals," New York, p. 310, 1908.

[96] Armsby, H. P., "The nutrition of farm animals." New York, p. 454, 1917.

[97] See, for example, Mayer, A., and Nichita, G., "Variation saisonnieres du metabolisme du lapin et modification de la fourrure," *Ann. de physichochim. biol.*, **5**, 621 (1929).

[98] Mitchell, H. H., and Haines, W. T., *J. Agr. Res.*, **34**, 549 (1927). Gerhartz, H., *Pflüger's Arch. physiol.*, **156**, 1 (1914).

[99] Capstick, J. W., and Wood, T. B., *J. Agr. Sci.*, **12**, 257 (1922). Deighton, T., *Id.*, **19**, 140 (1929).

[100] Forbes, E. B., Braman, W. W., and Kriss, M., *J. Agr. Res.*, **33**, 579 (1926).

Interesting as these "critical" values may be theoretically and for research purposes, they are probably without significance for normal farm animals under normal management conditions systems. There is need, as a basis for designing farm structures and air-conditioning, for mapping the temperature curve of heat and moisture dissipation under normal farm conditions.

At present we can employ only general considerations, which indicate that in most of this country elaborate barns are not needed for cattle, sheep, or horses—merely open sheds for protection against snow, rain, and wind.

11.6.4: Effect of hot weather on productivity and efficiency. As previously noted, sweating animals can withstand much higher temperatures than non-sweating. In non-sweating animals, at any rate in cattle, the body temperature is already above normal at environmental temperature [80° F (27° C)] (Figs. 11.10 and 11.17). Rise in body temperature is associated with a rapid rise in heat production or maintenance cost (Fig. 11.16, increasing rectal temperature by 4° F or 2.2° C doubled the heat production), and decline in productivity, as shown in Fig. 11.17, plotted from Regan[101]. When the environmental temperature was increased from 60° to 95° F (from 16° to 35° C), the rectal temperature of the cow increased from the normal 101° F level to approximately 104° F (from 38° to 40° C); the daily milk yield declined from 27 to 17 lbs.; the casein declined from 2.1 to 1.8 per cent; and the solid-not-fat declined from 8.1 to 7.6 per cent. The seriousness of the damage of high environmental temperature to milk production is evident from the fact that temperatures of 80° to 100° F are quite common in our richest agricultural regions, especially in the corn belt, where the temperature often rises to 110° F (43° C). Fig. 11.18 represents the depressing

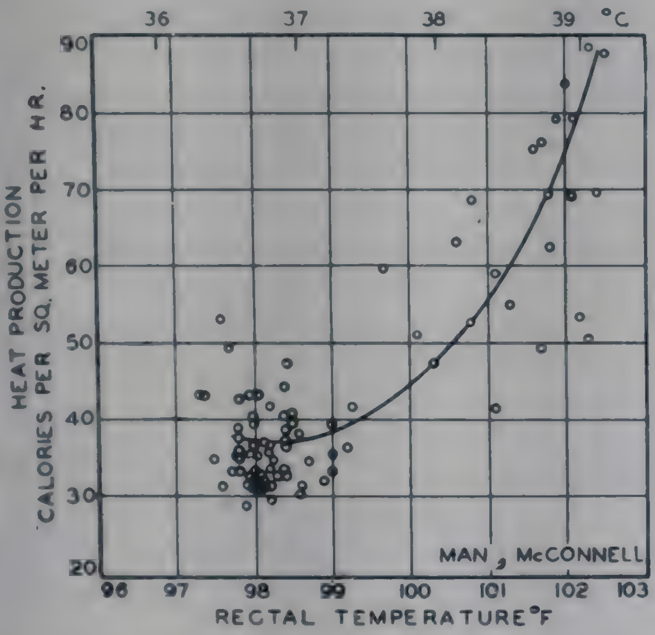

Fig. 11.16. Relation between rectal temperature and heat production in man plotted by us from data by McConnell,

influence of high environmental temperatures on feed consumption and feed utilization[102].

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[101] Regan, W. M., Richardson, G. A., *J. Dairy Sci.*, **21**, 73 (1938).

High temperature also depresses growth. Fig. 11.19 shows[103] the precipitate decline in growth of chickens during a hot July in Columbia, Missouri, when the maximum daily temperature rose to 110° F (43° C) and the mean daily temperature to 98° F (37° C).

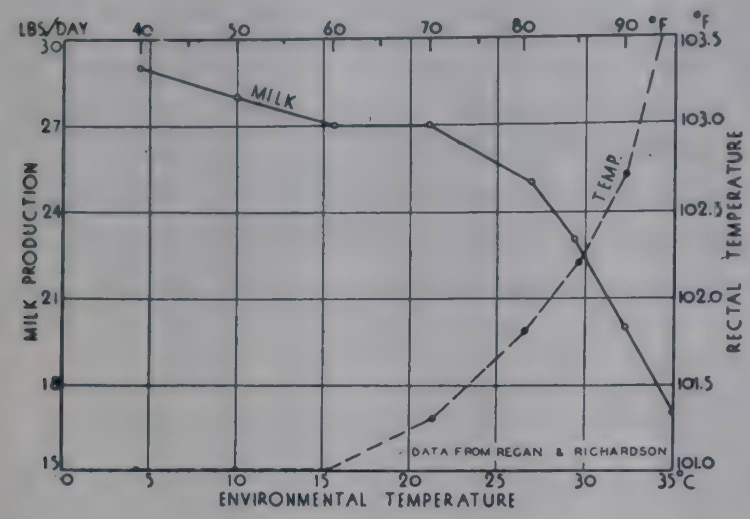

Fig. 11.17. Influence of environmental temperature on rectal temperature and on milk production in Jersey cattle.

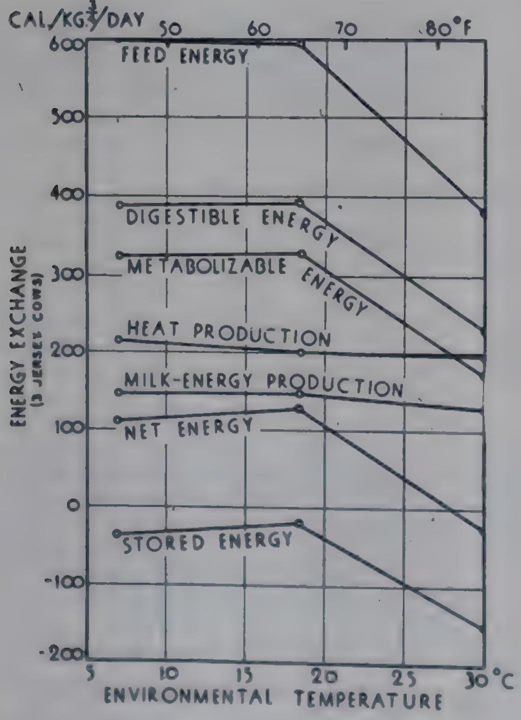

Fig. 11.18. Influence of environmental temperature on feed consumption, heat production, and feed utilization in dairy cattle. (From Kleiber.)

Fig. 11.20 shows the influence of environmental temperature on growth of chicks one to two weeks of age[104]. This growth rate is maximum at the surprisingly low temperature of 70° F (21° C).

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[102] Fig. 11.18 was generously furnished for this book by Dr. M. Kleiber who said that this chart was originally exhibited by M. Kleiber, G. A. Richardson, and W. M. Regan at the 1934 (Ithaca, N. Y.) meeting of the Am. Dairy Sci. Assn.

[103] Kempster, H. L., and Parker, J. E., "The normal growth of chickens under normal conditions," Univ. Missouri Agr. Exp. Sta. Res. Bull., 247, 1936.

The water-loss-temperature diagram for the domestic fowl[105] indicates that in the fowl thermoneutrality is close to 75° F (24° C) and that the body temperature must rise following 85° F (30° C) and certainly above 90° F (32° C).

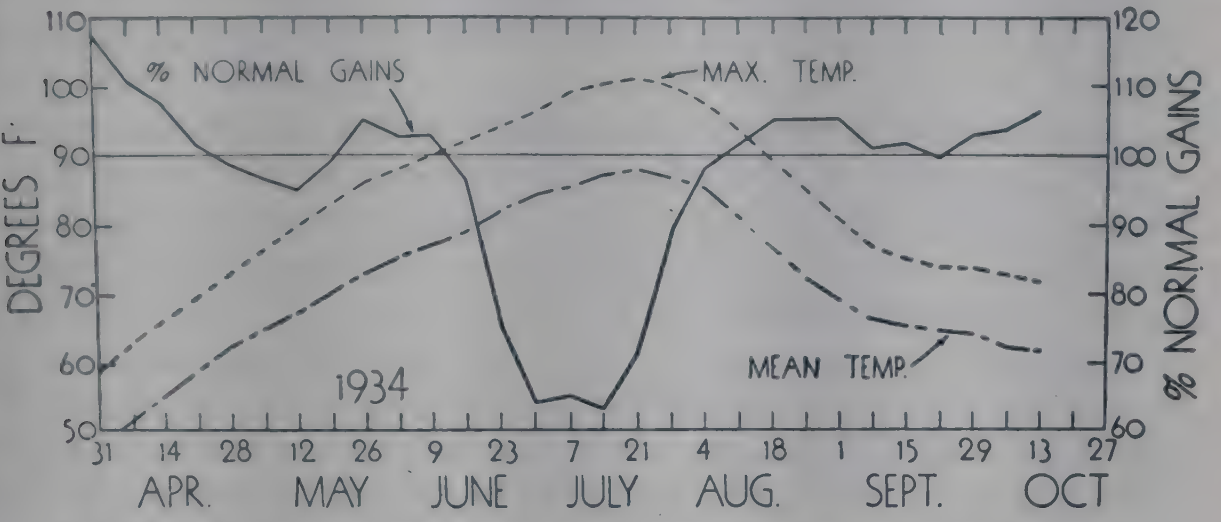

Fig. 11.19. Influence of environmental temperature on growth of chickens.

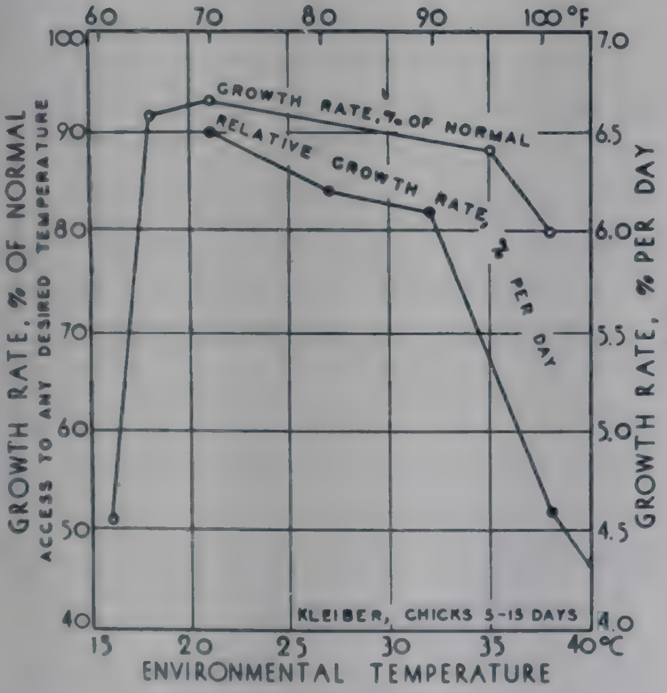

Fig. 11.20. Influence of environmental temperature on growth of chicks in a constant-temperature cabinet.

Cattle native to hot countries endure hot environments better than those native to temperate countries, and this may be true of other species. Thus

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[104] Kleiber, M., and Dougherty, J. E., *J. Gen. Physiol.*, **17**, 701 (1934). Winchester, C. F., and Kleiber, M., *J. Agr. Res.*, **57**, 529 (1938). See also Giaja, J., and Gelineo, S., "Facteur thermique de la croissance des homeothermes," *Bull. Acad. Roy. Serbe Sci. Math. nat.*, **1**, 103 (1933).

[105] Barott, H. G., and Pringle, E. M., *J. Nut.*, **22**, 273 (1941).

Zebu, or Brahman cattle, *Bos Indicus*, stand heat better than the European cattle, *Bos Taurus*[106], probably because the Indian cattle have more sweat glands than European cattle, just as human natives of hot climates probably have more sweat glands per unit skin area than natives of cold climates.

There is considerable literature on the influence of temperature on reproductive behavior.[107] The reproducing ability declines with rising temperature above 80° F.

Warren and associates discussed the influence of temperature on egg-shell thickness[108], egg size[109], blood calcium[110], and growth of the hen's ovum[111]. Shell thickness, blood calcium, and egg size decreases with rising environmental temperature above 70° F, and the birds consumed 26 per cent less feed on raising the temperature from 60° to 95° F.

It is customary to correlate milk production and milk composition with season (see Fig. 8.9). It is doubtful, however, whether the cow is a photoperiodic or thermoperiodic animal, and the seasonal milk-productivity rhythm is due to the injurious effects of overheating an animal not adopted to cope with hot weather.

11.6.5: Artificial cooling of non-sweating animals in hot weather. Since overheating in non-sweating animals is due to lack of skin moisture for vaporization, the obvious method for cooling would seem to be external application of moisture. Swine naturally resort to mud wallows for moisture in the desirable form of mud. When given the opportunity, cattle stand in cool water during hot weather, and sheep migrate to higher altitudes.

Under commercial conditions these summer devices are not usually accessible. Commercial air conditioning is too expensive, although consideration is given it[112]. Dairymen install powerful fans on the theory that fans cool cows as they do men. It is obvious from what has been said that this theory cannot be altogether true. Fanning cools sweating animals because it accelerates the vaporization of the sweat; but fanning cannot increase the vaporization rate if the skin is dry and cannot cool the animal unless the environmental temperature is lower than the skin temperature. The (sweating) dairyman's assumption that because he is cooled by fans the (non-sweating) cow is likewise cooled is understandable but not penetrating. Fans are not likely to increase the vaporization rate from the respiratory passages because the moisture from these sources is already fanned by the respiratory movements.

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[106] Rhoad, A. O., *Proc. Am. Soc. Animal Prod.*, p. 284 (1938); Kelley, R. B., Zebu (Brahman) Cross cattle. Council of Scientific Industrial Research, Commonwealth of Australia, Bul. 27, 1932. Kelley, M. A. R., "Basic problems in air conditioning of stables," Paper read at the St. Paul (June 1939) meeting Am. Soc. Agr. Engineers.

[107] McKenzie, F. F., and Berliner, V., "The reproductive capacity of rams," Univ. Missouri Agr. Exp. Sta. Res. Bull., 265, 1937. Phillips, R. W., and McKenzie, "The thermoregulatory function and mechanism of the scrotum," *Id.* Res. Bull., 217, 1934. Moore, C. R., "Heat application and testicular degeneration. The function of the scrotum," *Am. J. Anat.*, **34**, 337 (1934).

[108] Warren, D. C., and Schnepel, R. L., "The effect of air temperatures on egg-shell thickness in the fowl," *Poultry Sci.*, **19**, 67 (1940).

[109] Warren, D. C., "The effect of temperature on the annual egg-size curves of pullets kept at different latitudes," *J. Agr. Res.*, **59**, 441 (1939). Bennion, N. L., and Warren, D. C., "Temperature and its effect on egg size in the domestic fowl," *Poultry Sci.*, **12**, 69 (1933).

[110] Conrad, R. M., 'The effect of high temperature on blood calcium of the laying hen," *Poultry Sci.*, **18**, 327 (1939).

[111] Warren, D. C., and Conrad, R. M., "Growth of the hen's ovum," *J. Agr. Res.*, **58**, 875 (1939).

[112] Kelley[106]

It is true that even non-sweating animals give off some moisture from the skin[113]; Jersey cows are said[101] to give off about 1 pound of moisture per hour by non-sweating methods. However, this non-sweating moisture, referred to as diffusion or osmotic moisture[75] is probably unimportant in body-temperature regulation in hot weather (Fig. 11.17).

The foregoing discussion suggests the desirability of employing some substitute for sweat glands, perhaps some spongy, porous covering, such as rubber or acetate sponge, which holds moisture and permits good air circulation. A cover of some such fabric as jute may be useful to protect the rubber against sun and manure and assist with absorption and vaporization of the moisture. We investigated in a preliminary way the influence of wet, porous rubber sponge blankets on the respiration rate (the best index of a non-sweating animal's comfort with respect to temperature) of sheep and cows, with promising results, shown in Figs. 11.19 and 11.20.

Fig. 11.21 shows the results for sheep. Wet blankets were put on sheep A and B at 10:30 while sheep C and D served as controls. In the blanketed animals, the respiration rate immediately dropped from its initial level of about 190, to 160, 150, and finally 145. By 1 o'clock the blanket began to dry, and the respiration rate began to rise. When the blanket was removed, the respiration rate promptly attained its initial level. The environmental temperature during this observation was between 90° and 100° F (32° to 38° C).

Fig. 11.22 exhibits similar results for cattle. Four cows were observed. Cows 731 and 740 were not blanketed; cow 731 had a powerful fan blowing over her, while cow 740 had no fan. Cows 712 and 677 had wet sponge blankets; 712 had in addition a fan blowing over it; 677 had no fan. Under the given conditions, the fans apparently did not help either the blanketed or non-blanketed animals. Indeed, in the non-blanketed animals, the fan seemed to increase the respiration rate for a time, perhaps by forcing the hot air into the animal's skin. There is no doubt, however, that the wet blankets reduced the respiration rate considerably. It appears from these preliminary observations that a wet-porous blanket might maintain the comfort and productivity of non-sweating farm animals in the hot season of the year, thus preventing an enormous aggregate waste from declined productivities during July, August, and September.

11.6.6: Fever: heat exhaustion: heat cramp: ventilation and air-conditioning: exercise: diet: clothing: and weather. Most fevers reflect disturbance of the normal equilibrium between thermogenesis and thermolysis, a change in level of thermostatic control.

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[113] Richardson[74]

Malarial fever illustrates a different situation. Shivering during the chill increases heat production about three-fold, from about 80 to 230 Cal per hour[114]; yet heat elimination is not increased. The result is a rise in body temperature of about 2° C in one-half hour. At the beginning of the chill, the body temperature (of mouth or rectum) is normal, but the skin temperature is below normal, which gives the *sensation* of chill and leads to shivering. This illustrates the complicated temperature-gradient configuration. There may be a rise of temperature in one part and a decline in another, but one *feels* the temperature only of the part (skin) which is capable of signalling to the brain. The liver has a temperature which is normally several degrees above the rectal temperature, while the mouth temperature is about 1° C below the rectal.

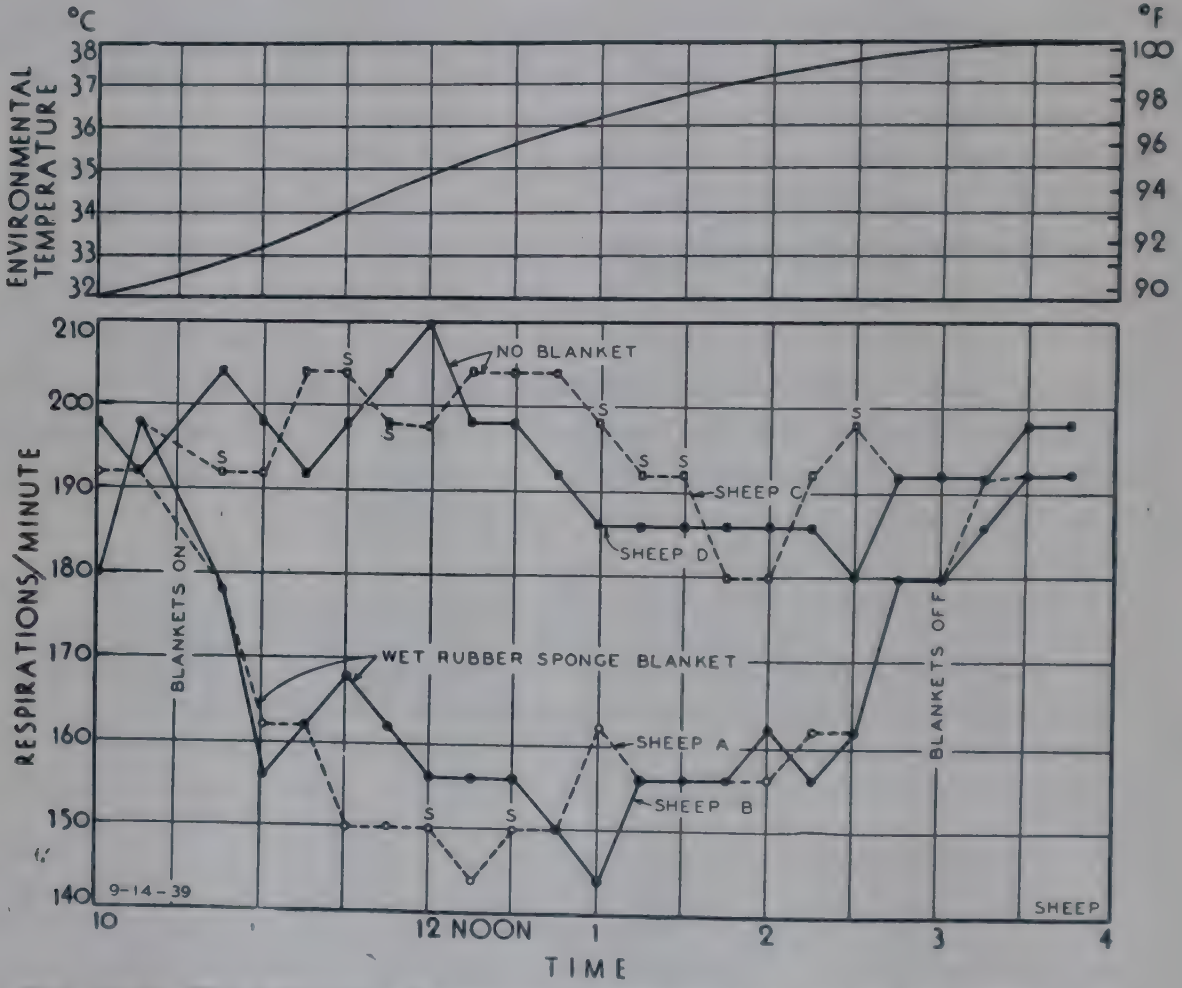

Fig. 11.21. The influence of a wet rubber-sponge blanket on the respiration rate of sheep.

The upper survival temperature limit for fever in man[115] is 107° F (41° C) but may rise in premortal states to 110° F (43° C). Each disease has its characteristic temperature curve: the temperature in malaria fluctuates; the temperature in pneumonia rises steadily until the crisis is reached. Fever may be produced not only by disease organisms, but also by chemical pyrogens, such as by dinitrophenols, thyroxine, and also by bacilli, dead or alive, and by other foreign bodies[116].

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[114] Barr, and Du Bois, *Arch. Int. Med.*, **29**, 608 (1922); **21**, 627 (1918). Du Bois, Harvey Lecture, Dec. 15, 1938. *Bull. N. Y. Acad. Med.*, **15**, 143 (1938). Du Bois, "Mechanisms of heat loss and temperature regulation," *Stanford Univ. Public Med. Sci.*, **5**, 315 (1937).

[115] *Cf. J. Am. Med. Assn.*, **110**, 459 (1938).

Elevation of body temperature may result from a hot environment or from excessive heat production consequent to hard muscular exercise. Such elevation of body temperature is often followed, especially in the aged, by collapse variously referred to as *heat exhaustion*, *heat stroke*, and *sun stroke*. The collapse may be due to the high temperature but more often to circulatory failure[117], partly as result of peripheral vasodilation with consequent necessity of accelerated circulation of the diminished available blood (the blood that is released for cooling at the body surface is, for the moment, unavailable for oxygen transport).

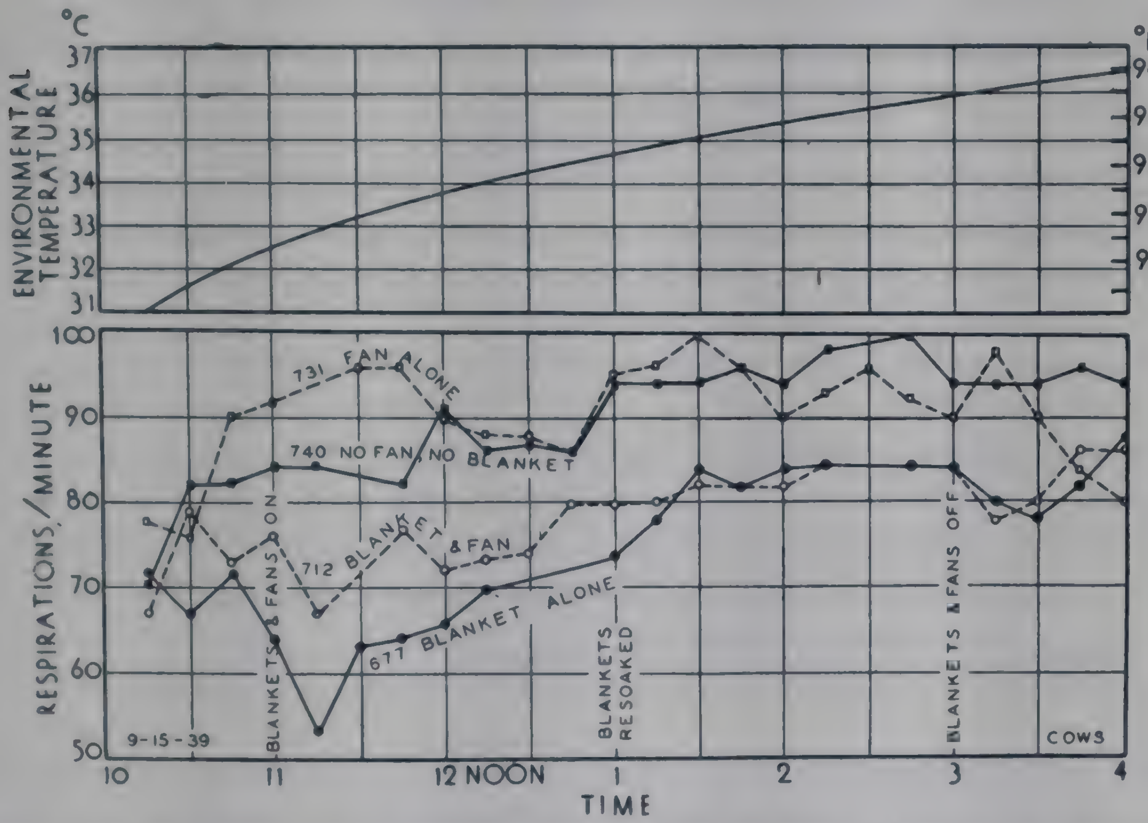

Fig. 11.22. The influence of a wet rubber-sponge blanket, and of fanning the uncovered and sponge-covered animals, on the respiration rate of cattle (Holsteins).

It is interesting to note that ascorbic acid (vitamin C) is excreted in sweat[118]; hence the greater need of vitamin C in profusely sweating persons. No doubt, the same holds true for other water-soluble vitamins and salts, which may lead to other disorders such as *heat cramp*.

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[116] For review, see Brody, S., *Ann. Rev. Biochem.*, **3,** 341 (1934).

[117] Shattuck, G. C., and Hilferty, M. M., "Sunstroke and allied conditions in the United States," *Am. J. Tropical Med.*, **12,** 223 (1932); *New England J. Med.*, **209,** 319 (1933). Bock, A. V., and Dill, D. B., "Physiological reactions to high environmental temperatures," *Id.*, **209,** 442 (1933). Hutt, F. B., "Susceptibility of chickens to extreme heat," *Poultry Sci.*, **17,** 454 (1938). Wilson, G., "The cardiopathology of heat stroke," *J. Am. Med. Assn.*, **114,** 557 (1940).

[118] Bernstein, R. E., *Nature*, **140,** 684 (1937).

A dramatic hot-weather disability in sweating animals in *dry* environment is *heat cramp*. The outstanding symptom is pain in the muscles, including the heart muscle. This results from excessive loss of common salt in the sweat[119]. This difficulty is prevented by drinking water containing[119] 0.1 per cent sodium chloride, and acute cases are cured by injection of large amounts of normal saline. It has been suggested to drink water containing 0.012 per cent KCl and 0.018 per cent NaCl. Farm animals that have access to salt probably never develop heat cramp, because, unlike man, animals develop a salt craving, and consequently satisfy the salt need.

However, administration of salt is not helpful in heat stroke, previously described, because the underlying difficulty is not salt loss but high body temperature and consequently high pulse rate (above 135).

For hot-weather comfort one should obviously avoid conditions that increase heat production and adopt those that protect against direct sunlight and increase heat dissipation. Heat production is, of course, increased by muscular exercise and high-protein food (*SDA*).

Protection against sun radiation includes such devices as wearing sun helmets; protecting windows by aluminum-painted awnings or venetian blinds—placed on the outside; protecting the roof, if flat, by a layer of water, otherwise by light-colored paint, preferably aluminum paint which absorbs only 40 per cent of the radiations as contrasted to asbestos shingles, unpainted wood, stone, brick, red tile, which absorb 70 per cent, and black surfaces, as slate or tar, which absorb 90 per cent of the radiations[120]. Water sprayed over the roof, and attic ventilation help to dissipate the absorbed heat.

The temperature of a room may be lowered directly by vaporization. The War Department uses[121] a cooler which consists of a metal cabinet filled with a fine porous substance, such as excelsior, thoroughly wet, and placed in the window. A fan on the roomside of the cabinet draws the wet air through the room. Evaporation of this moisture lowers the room temperature. This method, no doubt excellent for hot, dry climates, would not seem useful for hot, humid climates. Hot weather comfort depends on low relative humidity[122].

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[119] Talbot, J. H., and Michelson, J., "Heat cramps," *J. Clin. Inv.*, **12,** 533 (1933). Wilcox, W. H., *British Med. Jr. I.*, **392** (1920). Dill, D. B., Edwards, H. T., Bauer, P. S., and Levenson, E. J., *Arbeitesphysiol.*, **4,** 508 (1931). Dill, *Ann. Rev. Physiol.*, **1,** 551 (1939); also *Physiol. Rev.*, **16,** 263 (1936). Dill, D. B., Bock, A. V., Edwards, H. T., and Kennedy, P. H., *J. Ind. Hyg. and Toxicol.*, **18,** 417 (1936). Also: Moss, K. N., *Proc. Roy. Soc.*, **95B,** 181 (1924); Haldane, J. B. S., "Possible worlds," Harpers, 1928.

[120] Rowley, F. B., *Sigma Xi Quarterly*, **27,** 147 (1939).

[121] *J. Am. Med. Assn.*, **117,** 537 (1941).

[122] Relative humidity is the ratio of water vapor in the air to the maximum it can hold. As the water-holding capacity declines with fall of temperature, decline of temperature leads to condensation of moisture. Thus at 68° F (20° C) air holds 7.5 grains water

The importance to sweating animals of the effect of relative humidity on the cooling properties of air in hot weather may be inferred from the fact that while a man can hardly bear an environmental temperature of 98° F (37° C) in a saturated atmosphere, he can withstand for a short time a temperature of 150° F (65° C) in perfectly dry, briskly-moving air. Hence for practical comfort in hot weather, briskly moving dehumidified air may be as good as an atmosphere chilled by refrigeration. Chilled air often gives a feeling of stuffiness, and does not meet the need for a desirable variety in air movement and temperature, simulating the natural conditions of play of the wind, which invigorates and gives a feeling of freshness. As previously noted, for non-sweating animals briskly moving air may not be helpful, unless the surface of the animal is kept moist by some such device as a wet blanket or by sprinkling.

Some of the foregoing hot-weather suggestions may be reversed for comfort in cold weather. In cold weather foods or feeds having a high *SDA* effect (such as high protein) are desirable; so is exercise. Poorly insulated walls and ceilings give an unpleasant sensation of cold beyond the expectation of the physical temperature of the atmosphere. This is because cold walls cause excessive heat loss by radiation and one does not feel comfortable when the heat lost by radiation exceeds 50 to 60 per cent of the total heat produced. Room air at 60° F with walls at 80° F *feels*[123] as warm as room air at 80° F with walls at 60° F. Hence the importance for winter comfort of having well-insulated walls and ceilings. In frame houses walls are insulated by filling studding spaces with insulating material and using tightly fitting storm sashes.

High humidity in cold weather increases the feeling of cold because it increases the conductivity of clothing.

Clothing furnishes man with a private climate. The degree of privacy depends on the amount of air that the fur, feathers, or clothing can hold stationary. Fur is warm because of the great amount of air it holds. A good fur is composed of 98 per cent air and 2 per cent hair. The amount of air held in the fur or feathers is controlled by the animal by holding the hairs more or less erect. The more erect, the more air. The following figures give an idea of the relative conductivity (inverse of insulation) of air, hair, feather, and some fabrics[124]: air, 100; feathers, 108; knitted wool, 122; smooth silk fabric, 129; hair, 143; smooth cotton fabric, 152; linen, 218; water, 2000.

From the high conductivity and latent heat of water, the importance of

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vapor; at 50° F (10° C) it holds only 4.2 grains, and the remaining 3.3 grains drops out as liquid water. Hence cold walls tend to be wet. At 70° F (21° C), 30 to 60 per cent relative humidity is most comfortable.

[123] See Yaglou, C. P., "The effective temperature index," *J. Ind. Hygiene*, **9**, 297 and 251 (1927); **10**, 350 (1928); *J. Am. Med. Assn.*, **108**, 1708 (1937). Winslow, C-E. A., *J. Public Health*, **27**, 767 (1937).

[124] O'Brien, Ruth, "Bibliography on the relation of clothing to health," U.S.D.A. Miscellaneous Pub., 62, 1929.

knowing the relative absorbtion and vaporization properties is evident. Yarn construction and weave make a great deal of difference. As regards water absorption, the following are probably in decreasing order: sponge rubber, linen, cotton, silk, jute. Little is known concerning the relative ease with which moisture is given off by various substances. All that can be said is that densely woven materials do not absorb moisture. Feathers and wool are naturally covered with oil, which repels moisture. For hot-weather wear, the clothing should be porous so as to absorb moisture from the skin and then give it off slowly for comfortable cooling of the body. This reasoning justifies woolen underwear in hot weather.

It is interesting to note that under the same environmental condition of 72° F (22° C), relative humidity 30 per cent, and air movement 20 feet/minute, the mean skin temperature of woman is 2° F lower than of man, and that of the hands and feet 5° F lower. Under these conditions men feel comfortable and women feel cool. Room temperatures of 71.5° F for men and 76° F (25° C) for women give the same skin temperature (92° F) and comfort to both.[125] In the nude and in basal condition men have a slightly higher skin temperature than women,[126] probably due to differences in subcutaneous fat. In summer weather of 94° F (34° C) the skin temperature is the same in both.

These sex differences in skin temperature and comfortable feeling seem to be due mostly to sex differences in clothing worn and, to a slight extent, to differences in subcutaneous fat. In general, when men and women wear the same clothing, the skin temperature and comfortable feeling are virtually the same for both. With minimum clothing, 82° F (giving a mean skin temperature of about 93° F), satisfies both equally well.

Fairly hard muscular work, such as mining and farming, is best done not at thermoneutrality but at the relatively low temperatures of 40° to 65° F (4° to 18° C). One cannot, however, speak of temperature independently of humidity and air movement, since the three are interrelated in their physiologic effects. The "effective temperature" represents physiologic effect[127]. Pending the more general adoption of the effective temperature scale, 65° F (18° C) is currently quoted as the minimum suitable temperature during rest for man, but the most comfortable condition is nearer 75° F (24° C), depending on the season (acclimatization).

Productive farm animals are in the condition of hard-working men, doing best below 65° F (18° C), and the published "critical temperatures" for farm animals have no bearing on the temperature of maximum productivity and efficiency. The serious agricultural problem in most parts of this country is not how to keep adult farm animals warm in winter but how to keep them cool in summer.

11.7: Summary. The major concerns of this chapter are: (1) the mechanism of homeothermy, and (2) the influence of environmental temperature on the speeds and efficiencies of life processes in animals, with applications to calorimetry and animal husbandry. Brief consideration is also given to the influence of environmental temperature on the physiologic reactions of man.

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[125] Yaglou, C. P., *J. Am. Med. Assn.*, **117**, 1261 (1941).

[126] Hardy, J. D., and Du Bois, E. F., *Proc. Nat. Acad. Sci.*, **26**, 389 (1940).

[127] Farderber, M. B. F., and Houghten, F. C., "Effective temperature scales," *J. Am. Med. Assn.*, **116**, 474 (1941).

Homeothermy is achieved by a number of devices including: (1) cooling by vaporization of moisture from the respiratory passages and skin (a curious fact in this connection is that the rate of respiration in non-sweating animals increases according to the Van't Hoff-Arrhenius equation with respect *not* to body temperature, as might be expected, but to environmental temperature); (2) developing insulating coatings (fat, fur, etc.) on approach of the cold season; (3) dilation or contraction of surface blood vessels by nervous mechanisms, thus exposing the blood to the surface for cooling, or removing from the surface for protection from cold; (4) changing the blood volume and blood concentration; (5) varying the rate of production of metabolic hormone (acetocholin, adrenaline, thyroxine); and (6) changing tonus of muscles, thus changing the rate of heat production; (7) adopting certain behavior patterns (huddling, rolling up, spreading out, etc.).

According to their ability to withstand high environmental temperature, homeotherms are divided into (1) profusely sweating animals, exemplified by men, horses, mules, and asses, who can withstand great heat, particularly in dry, moving air; (2) slightly sweating (or panting) animals, exemplified by cattle, sheep, swine, dogs, cats, rats, and rabbits, unable to withstand great heat.

When a profusely sweating animal is placed in a hot environment it responds by sweating, and by sending its blood to the moist surface for cooling by vaporization of the sweat. This reduces the blood volume needed for carrying oxygen to the tissues. To compensate for this deficiency, the heart pumps faster, that is, the *pulse rate rises*. When a slightly sweating animal is placed in a hot environment, it responds not so much by sweating as by panting, that is, by a rapid but shallow respiration rate. The skin is not cooled because it is relatively dry, and the blood is sent from the hot skin to the interior, with the result that the *pulse rate declines*. As the increased respiration rate in hot weather does not increase the vaporization rate to the same extent as sweating does, the slightly sweating animal becomes overheated at relatively low temperatures, with consequent increase in heat production (maintenance cost), decrease in productivities, and decrease in efficiencies of the productive processes. Practical suggestions are presented for cooling non-sweating animals in hot environments by the use of wet, porous, sponge-and-fabric blankets as substitutes for sweat glands.

Beginning with the "comfort zone", farm animals, especially of the non-sweating class, are very much less sensitive to declining than to rising temperature. Thus the productivities, efficiencies, and comfort of farm animals are not reduced by decline in the environmental temperature from the comfort zone of 60° to 70° F (15-21° C) to perhaps 0° F, while raising the temperature above 80° F overheats and seriously reduces the productivities of non-sweating farm animals, and to a less extent of sweating animals. Homeotherms have much more powerful methods for protection against cold than heat.

Similarities and differences between the influence of environmental temperature on productivities and efficiencies of homeotherms and poikilotherms are brought out, with special reference to the operation of the Van't Hoff law in the two classes of animals, as illustrated by decline in metabolism in poikilotherms and rise in homeotherms when the temperature falls below about 80° F or 27° C.

Chapter 12

Methods in Animal Calorimetry

> The modern era of the science of nutrition was opened by Lavoisier in 1780. Lavoisier (1743–1794) was the first to recognize that animal heat was derived from the oxidation of the body's substance and he compared animal heat to that produced by a candle. The form of Lavoisier's apparatus is illustrated in two drawings made by Madame Lavoisier. But the method is unknown, for on May 8, 1794, Lavoisier was executed by the Paris Commune.
> *Graham Lusk*

12.1: Principles. The two major biocalorimetric categories are *direct* and *indirect.* In the absence of anaerobic, endothermic, and other unusual reactions in which the caloric equivalents of O_2 and CO_2 are unknown, the results of the two methods are in substantial agreement. Both are equally simple in principle. In practice, since the direct method is much more expensive and complicated, it is rarely used, except when unusual metabolic reactions are suspected and the caloric values of O_2 or CO_2 are in doubt.

Both direct and indirect methods were originated by Lavoisier[1, 2] in a year memorable in American and French history, 1777. Lavoisier then introduced the essentially modern chemical nomenclature, especially as it relates to oxygen in life processes, and demonstrated that living involves oxidation. He defined life as a chemical process: "*La vie est une fonction chimique*". Lavoisier is thus the founder of modern nutrition as well as of modern chemistry.

12.1.1: Direct calorimetry. Lavoisier and Laplace confined a guinea pig in a chamber containing a given weight of ice, and estimated the heat production from the amount of ice melted. The carbon dioxide exhaled was also collected. They found that the melting of a given weight of ice corresponds to the exhalation of a definite amount of carbon dioxide. They also measured the heat production of a rabbit by the temperature rise in a given volume of water surrounding the animal chamber. Modern animal calorimeters apparently differ only in detail from the Lavoisier models.

About ¼ of the body heat is dissipated by moisture vaporization which can be measured by absorption in such reagents as H_2SO_4, $Mg(ClO_4)_2$, and so on. About ¾ of the heat is emitted by radiation, conduction, and convection, and can be measured by absorption in water. The total heat produced is the sum of the two.

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[1] See Lusk, G., "The science of nutrition," 1928, Chapter 1, for a fascinating historic outline of Lavoisier's contributions.

[2] Lavoisier, A. L., "Expériences sur la respiration des animaux et sur les changements qui arrivent à l'air en passant par leur poumons," Mém. de l'Acad. des Sci., 1777 (also in "Oeuvres de Lavoisier," Vol. 2). Lavoisier, A. L., et Laplace, "Mémoire sur la chaleur", "Mém. de math. et de phys. de l'Acad. d. Sci", 1780 Lavoisier, "La traité élémentaire de la chimie", 1780.

The modern water calorimeter is a well insulated box, just large enough to hold the subject. The inside of the box is usually lined with copper, the outside with zinc. The two are connected by resistance thermometers so as to keep the outside zinc lining at the same temperature as the inside copper lining, thereby avoiding loss of heat from the calorimeter.

The chamber interior is kept at a constant temperature by water circulating through pipes attached to the ceiling. The heat absorbed by the water is computed from the amount of water flowing per unit time, and from the temperature difference between incoming and outgoing water. Thus, if 20 kg water flows per hour, and the temperature of the water is 1°C higher at the exit than at the entrance, the heat absorbed by the water is 20 Cal. The heat of vaporization is determined by the weight increase of the water absorbers. The vaporization of 1000 grams (1 liter) of moisture is equivalent to 580 Cal. heat dissipation.

In compensation calorimetry[3] one chamber holds the animal while another, similar chamber has electric-resistance wires made to produce exactly the same amount of heat as that emitted by the subject in the other chamber. In differential calorimetry[4] the rate of total heat supply is maintained constant, first with the calorimeter empty, second with the animal inside.

The first modern respiration calorimeter was built by Max Rubner for a dog. It was provided with an open-circuit (Pettenkofer-Voit) apparatus. In this way, Rubner[5] demonstrated in 1894 that the heat measured by direct calorimetry is in substantial agreement with the heat computed from indirect calorimetry. This was amply confirmed.[6]

12.1.2: Indirect calorimetry. Indirect calorimetry was first used by Lavoisier and Laplace, who demonstrated that the exhalation by a guinea pig of a given quantity of carbon dioxide corresponds to the melting of a given weight of ice surrounding the animal. Indirect calorimetry is thus based on the fact that, normally, O_2 consumption and CO_2 production are closely correlated with heat production. This may be illustrated by the oxidation equation for carbohydrate previously discussed (Ch. 2).

$$\begin{array}{lllllll} C_6H_{12}O_6 & + & 6O_2 & = & 6CO_2 & + & 6H_2O + 678 \text{ Cal} \\ 180 \text{ g} & & 134.4 \text{ lit} & & 134.4 \text{ lit} & & \end{array}$$

The equation states in effect that the consumption of 6 mols (that is $6 \times 24.4 = 134.4$ lit) O_2, or the production of 6 mols CO_2, in the oxidation of a mol hexose (180 g) yields 678 Cal; therefore, the consumption of 1 lit O_2, or the production of 1 lit CO_2, yields for *carbohydrate oxidation* 5.047 Cal ($5.047 = 678/134.4$). The heat production may then be measured by liters O_2 consumed, or CO_2 produced, multiplied by 5.047. It may be shown

[3] Benedict, F. G., and Lee, R. C., Carnegie Inst. Washington Publ., 489, (pp. 14–16) (1937). Abderhalden's "Handb. d. biol. Arbeitsm," Abt. IV, Teil, **13**, p. 689 (1934). Hari, P., *Bioc. Z.*, **250**, 326 (1932); Gasnier, A., et Mayer, A., *Ann. Physiol.*, **8**, 633 (1932).

[4] Murlin, J. R., and Burton, A. C., *J. Nut.*, **9**, 233 (1935); Barrows, W. M., Jr., and Murlin, J. R., *Proc. Am. Phil. Soc.*, **78**, 483 (1938).

[5] Rubner, M., Die Quelle der tierischen Warme," *Z. Biol.*, **30**, 73 (1894).

[6] Atwater, W., and Benedict, F. G., "Experiments on the metabolism of energy and matter in the human body," U. S. Dept. Agr. Office Exp. Station, Bull., 69, 109, 136 (1899, 1902, 1903). Lusk, G., "The Science of Nutrition." Armsby, H. P., "Principles of Animal Nutrition."

in similar manner that for the oxidation of *mixed fat*, 4.69 Cal is generated per liter O_2 consumed, or 6.6 Cal per liter CO_2 produced.

For the oxidation of *mixed protein* 4.82 Cal is generated per liter O_2 consumed or 5.88 Cal per liter CO_2 produced. (Pflüger's "caloric coefficient of oxygen" is the ratio of heat produced in Calories to O_2 consumed in g, which is about 3.5 for carbohydrates, 3.3 for fat, and 3.2 for protein oxidation.)

Since the caloric equivalent of O_2 consumed and CO_2 produced varies with the nature of substance oxidized, it is theoretically necessary to know the composition of the fuel mix (carbohydrate, fat, protein) oxidized.

The amount of protein oxidized is computed from the urinary N excretion. Assuming that protein contains 16 per cent N and that all urinary N is derived from protein oxidation, the protein catabolized is estimated by multiplying the urinary N by 6.25 ($\frac{100}{16} = 6.25$). These assumptions are sufficient, although not literally true

Thus only $\frac{1}{3}$ to $\frac{1}{2}$ of potato N is in protein form. Alfalfa, as well as potato, contains many non-protein nitrogenous compounds, such as stachydrine, choline, adenine, trimethylamine, and betaine. Animal protein, such as casein, serum globulin, serum albumin, and also legume-seed protein contains 16 per cent N (conversion factor 6.25); cereal proteins contain 17–18 per cent N (conversion factor 5.8 to 5.9); oil-seed proteins contain 18–19 per cent N (conversion factor 5.3).[7]

The relative amounts of fat and carbohydrate oxidized are determined from the non-protein *respiratory quotient*, R.Q. The R.Q. is the ratio of mols or volumes of CO_2 produced to mols or volumes O_2 consumed. For the oxidation of carbohydrates the R.Q. is unity, as shown by the foregoing oxidation equation for carbohydrate,

$$\frac{6CO_2}{6O_2} = 1.00$$

Conversely, when the non-protein R.Q. is 1.00, it is assumed that carbohydrate is oxidized.

The R.Q. for *mixed fat* is 0.71, although each fat has its distinctive R.Q. The short-chain fats have an R.Q. nearer 0.8:

$$C_3H_5(CH_3CH_2CO \cdot O)_3 + 37O_2 = 30CO_2 + 26H_2O$$

$$\text{R.Q.} = \frac{30}{37} = 0.8$$

The long-chain fats have an R.Q. nearer 0.70:

$$2C_3H_5[CH_3(CH_2)_{15}CO \cdot O]_3 + 145O_2 = 102CO_2 + 86H_2O$$

$$\text{R.Q.} = \frac{102}{145} = 0.703$$

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[7] Jones, D. B., U. S. Department of Agriculture Circular, 183, 1931.

The R.Q. for *mixed protein* is 0.81, although, as fats, each protein and amino acid has its distinctive R.Q. The oxidation of the amino acid alanine may yield an R.Q. of 0.83. Thus

$$2CH_3CH(NH_2)_2COOH + 6O_2 = CO(NH_2)_2 + 5CO_2 + 5H_2O$$

$$R.Q. = \frac{5}{6} = 0.83$$

However, other amino acids and other conditions (Ch. 4) may yield different values.

TABLE 12.1.—Thermal Equivalents of O_2 and CO_2 and the Corresponding Percentages of Fat and Carbohydrates Oxidized for Different Respiratory Quotients (R.Q.)[8].

R.Q.	O_2 Cal/lit	CO_2		% O_2 Consumed by		% Heat produced by oxidation of	
		Cal/lit	Cal/gm	Carbohydrates	Fat	Carbohydrates	Fat
0.70	4.686	6.694	3.408	0	100	0	100
0.71	4.690	6.606	3.363	1.0	99.0	1.1	98.9
0.72	4.702	6.531	3.325	4.4	95.6	4.8	95.2
0.73	4.714	6.458	3.288	7.85	92.2	8.4	91.6
0.74	4.727	6.388	3.252	11.3	88.7	12.0	88.0
0.75	4.729	6.319	3.217	14.7	85.3	15.6	84.4
0.76	4.752	6.253	3.183	18.1	81.9	19.2	80.8
0.77	4.764	6.187	3.150	21.5	78.5	22.8	77.2
0.78	4.776	6.123	3.117	24.9	75.1	26.3	73.7
0.79	4.789	6.062	3.086	28.3	71.7	29.9	70.1
0.80	4.801	6.001	3.055	31.7	68.3	33.4	66.6
0.81	4.813	5.942	3.025	35.2	64.8	36.9	63.1
0.82	4.825	5.884	2.996	38.6	61.4	40.3	59.7
0.83	4.838	5.829	2.967	42.0	58.0	43.8	56.2
0.84	4.850	5.774	2.939	45.4	54.6	47.2	52.8
0.85	4.863	5.721	2.912	48.8	51.2	50.7	49.3
0.86	4.875	5.669	2.886	52.2	47.8	54.1	45.9
0.87	4.887	5.617	2.860	55.6	44.4	57.5	42.5
0.88	4.900	5.568	2.835	59.0	41.0	60.8	39.2
0.89	4.912	5.519	2.810	62.5	37.5	64.2	35.8
0.90	4.924	5.471	2.785	65.9	34.1	67.5	32.5
0.91	4.936	5.424	2.761	69.3	30.7	70.8	29.2
0.92	4.948	5.378	2.738	72.7	27.3	74.1	25.9
0.93	4.960	5.333	2.715	76.1	23.9	77.4	22.6
0.94	4.973	5.290	2.693	79.5	20.5	80.7	19.3
0.95	4.985	5.247	2.671	82.9	17.1	84.0	16.0
0.96	4.997	5.205	2.650	86.3	13.7	87.2	12.8
0.97	5.010	5.165	2.629	89.8	10.2	90.4	9.6
0.98	5.022	5.124	2.609	93.2	6.8	93.6	6.4
0.99	5.034	5.085	2.589	96.6	3.4	96.8	3.2
1.00	5.047	5.047	2.569	100	0	100	0

Table 12.1, after Lusk, originally (1901) after Zuntz and Schumberg, indicates the percentages of fat and carbohydrates oxidized and the caloric equivalents of O_2 and CO_2 for different non-protein R.Q. values; and Table

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[8] See Lusk, G., "The Science of Nutrition," Chapter 8, 1928. See also Zuntz, N., and Schumberg, H., "Studien zur einer Physiologie des Marsches Berlin," p. 361, 1901.

12.1A illustrates the method of computing heat production employing the R.Q. and urinary-nitrogen methods.

In most cases it is not necessary, often not even advisable, to employ the elaborate method given in Table 12.1A for estimating metabolism because the R.Q. does not always have the rigorous significance given it in the above considerations and in Table 12.1.

Thus, cattle and other ruminants produce huge quantities of CO_2 in the digestive tract (Ch. 2) by anaerobic bacterial fermentation and by liberation of CO_2 from bicarbonates. This extra-metabolic CO_2 cannot be distinguished from the respiratory-metabolism CO_2. Under such conditions the R.Q. has no metabolic significance, and, of course, the quantity of CO_2 production cannot be taken as a measure of metabolism. Under such conditions the rate of oxygen consumption is the best measure of heat production. Incidentally, under such fermentation conditions, direct calorimetry would not indicate with precision metabolism in the body proper, as it would include the heat of fermentation.

TABLE 12.1A.—Computing Energy Metabolism and Non-protein R.Q. from the Urinary N* and Respiratory Exchange.
(Data re-arranged from Lusk's book, p. 69 (1928) on a 12.75-kg dog)

(1) G urinary N excreted/hr	0.136
(2) G "protein" oxidized (1 × 6.25)	0.850
(3) G CO_2 associated with protein oxidation (1 × 9.35)	1.272
(4) G O_2 associated with protein oxidation (1 × 8.49)	1.15
(5) Liters CO_2 associated with protein oxidation (3 × .5087)	0.647
(6) Liters O_2 associated with protein oxidation (4 × .6998)	0.805
(7a) Total g CO_2 exhaled/hr	6.75
(7b) Total liters CO_2 exhaled/hr (7a × 0.509)	3.44
(8a) Total g O_2 consumed/hr	6.17
(8b) Total liters O_2 consumed/hr (8a × 0.6998)	4.32
(9) Liters non-protein CO_2 (7b − 5)	2.79
(10) Liters non-protein O_2 (8b − 6)	3.52
(11) Non-protein R. Q. (9/10)	0.79
(12) Overall R.Q. (7b/8b)	0.80
(Indicating that overall and non-protein R.Q. are not likely to differ much.)	
(13) Caloric value/lit O_2 at given R.Q. (0.79)	4.789
(14) Non-protein Calories (10 × 13)	16.86
(15) Protein Calories (1 × 26.5)	3.60
(16) Total Calories by indirect calorimetry (14 + 15)	20.46
(17) Calories by direct calorimetry	20.92
(18) Difference between direct and indirect calorimetry, 0.46 Cal, or 2.3 per cent	

* 1 g urinary N derived from protein is associated with the consumption of 5.91 liters or 8.49 g O_2 and the production of 4.76 liters or 9.35 g CO_2, and production of 26.5 Calories. $1 \text{ g } O_2 = 0.6998$ lit. $1 \text{ g } CO_2 = 0.509$ lit. The oxidation of 1 g fat (tripalmitin) is associated with consumption of 2.01 liters O_2 and production of 1.41 liters CO_2; the oxidation of 1 g starch is associated with the consumption of 0.83 lit O_2 and production of 0.83 lit CO_2. The non-protein R.Q. is estimated by deducting the liters of protein CO_2 produced (g urinary N × 4.76) from the total liters CO_2 produced, and the liters of protein O_2 consumed (g urinary N × 5.9) from the liters of total O_2 consumed.

Excess CO_2 may also be liberated under conditions of acidosis, such as ketosis, and of overventilation in general. On the other hand, CO_2 may be stored under conditions of alkalosis. A low R.Q. may also result from incomplete oxidation, formation of sugar from protein, fat, and other substances.

Moreover, as shown in Table 12.1, while the range in caloric equivalents of CO_2 is relatively wide, from 5.0 to 6.7 Cal per liter, the range of caloric equivalent of O_2 is relatively narrow, from 4.7 to 5.0 Cal per liter, an extreme range of 7 per cent, or a deviation of about 3.5 per cent from the mean value (when the R.Q. is 0.82), which is within the limits of experimental error in metabolism measurements.

Furthermore, since the average R.Q. of protein is 0.82, which corresponds to the average caloric value of O_2 of 4.825 Cal per liter, no correction need be made for protein metabolism when measuring energy metabolism by oxygen consumption. (Benedict reported 4.7 Cal per liter O_2 for protein.)

The simplest and, under normal conditions, perhaps the most accurate, method for measuring energy metabolism is, then, by the rate of oxygen consumption, as fed from a calibrated oxygen container, and computing the heat production by the caloric value of oxygen, *e.g.*, 4.825 Cal/liter, corresponding to an R.Q. of 0.82.

The basal metabolism in humans is measured about 12 hours after the preceding meal, when the R.Q. is about 0.82.

We[9] have adopted this method for measuring the energy metabolism of farm animals—cattle, horses, sheep, swine, and goats; and we have even measured the metabolism of elephants by this method[10], the results of which agreed satisfactorily with those published later by Benedict[11]. Let us describe this method of measuring metabolism in detail, after a brief summary.

To summarize, energy metabolism may be measured by (1) *direct calorimetry*, by absorption of the heat in a water jacket and collecting the expired moisture or by related methods; (2) *indirect calorimetry*, by measuring O_2 consumption alone, or in combination with CO_2 production and urinary-nitrogen excretion. For most purposes—when the reactions are not endothermic or partly anaerobic and the caloric equivalent of O_2 is known—indirect calorimetry is more reliable than direct, and the measurement of O_2 consumption alone gives as good, sometimes better, results[12] than measuring CO_2 production and the R.Q.

[9] Brody, S., Univ. Missouri Agr. Exp. Sta. Res. Bull., 143, 1930.

[10] Brody, S., and Procter, *Id.*, Res. Bull. 220, pp. 12 and 32, 1934.

[11] Benedict, F. G., "The physiology of the elephant," Carnegie Inst., Washington Publ., 474, 1936.

[12] For objections against O_2 consumption as index of metabolism and for the advantages of CO_2 as metabolic index, see Adams, T. W., and Poulton, E. P., *Guys Hosp. Repts.*, **85**, 56 (1935), and **87**, 107 (1937). King, J. T., *Johns Hopkins Hosp. Bull.*, **32**, 277 (1921). Rabinowitch, I. M., and Bazin, E. V., *J. Canadian Med. Assn.*, **16**, 638 (1926). Adams and Poulton: "CO_2 production is more constant with R.Q. change than is O_2 consumption; range in heat value of CO_2 is only apparent, not real, due to interconversion of fat and C.H.; CO_2 is a direct combustion product while changes in O_2 may be due to changes in fat–C.H. interconversions."

The *indirect* biocalorimetric methods are divided into (1) *closed-circuit type* (Regnault and Reiset, 1849), involving rebreathing the same air after removing its CO_2 by circulating through alkali [soda lime, $Ba(OH)_2$ solution, etc.] and replacing the consumed O_2 by fresh O_2; (2) *open-circuit type* (Pettenkofer and Voit, 1862), involving the circulation of outside air through the system. Examples of each system of measuring metabolism are described below.

12.2: Methods of indirect calorimetry. Since direct biocalorimetry is not often used, the discussion is confined to indirect methods.

12.2.1: Closed-circuit spirographic-mask method for farm animals. This method is illustrated in Figs. 12.1 to 12.7. Its use for measuring human "basal" (or "standard") metabolism was made generally known by Benedict[13] and associates. It consists in connecting the pulmonary system of the subject to an oxygen spirometer, and measuring the rate of oxygen consumption by the rate of decline of the oxygen bell. As shown in Fig. 12.1a, after Roth[13] and Collins[14], the air is circulated freely through the porous soda lime in one direction by the valves, *V*. The oxygen bell, *B*, which floats freely in the water seal, is counterbalanced by a weight, and so will not rise or fall except when acted upon by the circulating air. The decline of the bell is recorded graphically on the kymograph drum, *K*. The rate of oxygen consumption is computed from the slope of this graphic record.

Note from Fig. 12.3 to 12.6 that the animals are entirely at ease in natural positions, completely under the operator's control. There is thus no problem in "correcting" for standing and for other uncontrolled activities encountered by the use of the respiration-chamber method of measuring metabolism.

The clock-kymograph (*K* in Fig. 12.1) records the rate of oxygen consumption graphically. A typical graph is shown in Fig. 12.7. Note that the slope, not necessarily the absolute decline, in the oxygen bell, is used for computing the rate of O_2 consumption.

The oxygen bell (*B* in Fig. 12.1) is of a size to produce an oxygen-consumption line of reasonable slope (Fig. 12.7). The oxygen bell used for human metabolism by the Benedict-Roth method has a volume of 20.73 cc per 1 mm height. This oxygen volume has a caloric equivalent of 0.1 Cal (under STP conditions, assuming an R.Q. of 0.82 with a caloric equivalent of 4.825 Cal per liter). This bell size was adopted to facilitate computation. Roth measured the decline in slope for a 6-minute interval: a 1-mm slope per 6-minute interval corresponds to 0.1 Cal per 6 minutes, or 1.0 Cal per hour. Likewise, a 50-mm rise in 6 minutes corresponds to a heat production of 50 Cal per hour. Table 12.2 presents the relation between diameter, cross-section area, and cc per mm height of oxygen bell employed in our work.

When using the Benedict-Roth size spirometer the slope of the spirograph in mm per 6 minutes is multiplied by a factor to reduce it to standard temperature, pressure, and humidity (see Table 12.3). The resulting value corresponds to the heat production in terms of Cal per hour. If there is a temperature rise in the oxygen bell during the 6 minutes, $\frac{1}{2}$ mm per °C is added to the rise of the O_2 consumption line before the other computations are made. The oxygen-spirometer method for measuring metabolism was originated (1887) by Fredericq[15] and perfected by Benedict and associates[13] in the United States and by Krogh[16] in Europe.

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[13] Benedict, F. G., and Collins, W. E., *Boston Med. and Surg. J.*, **183**, 449 (1920); Roth, P., *Id.*, **184**, 222 and 228 (1921); **186**, 457, 491 (1922).

[14] Collins, W. E., 555 Huntington Ave., Boston, Massachusetts, maker of metabolism apparatus.

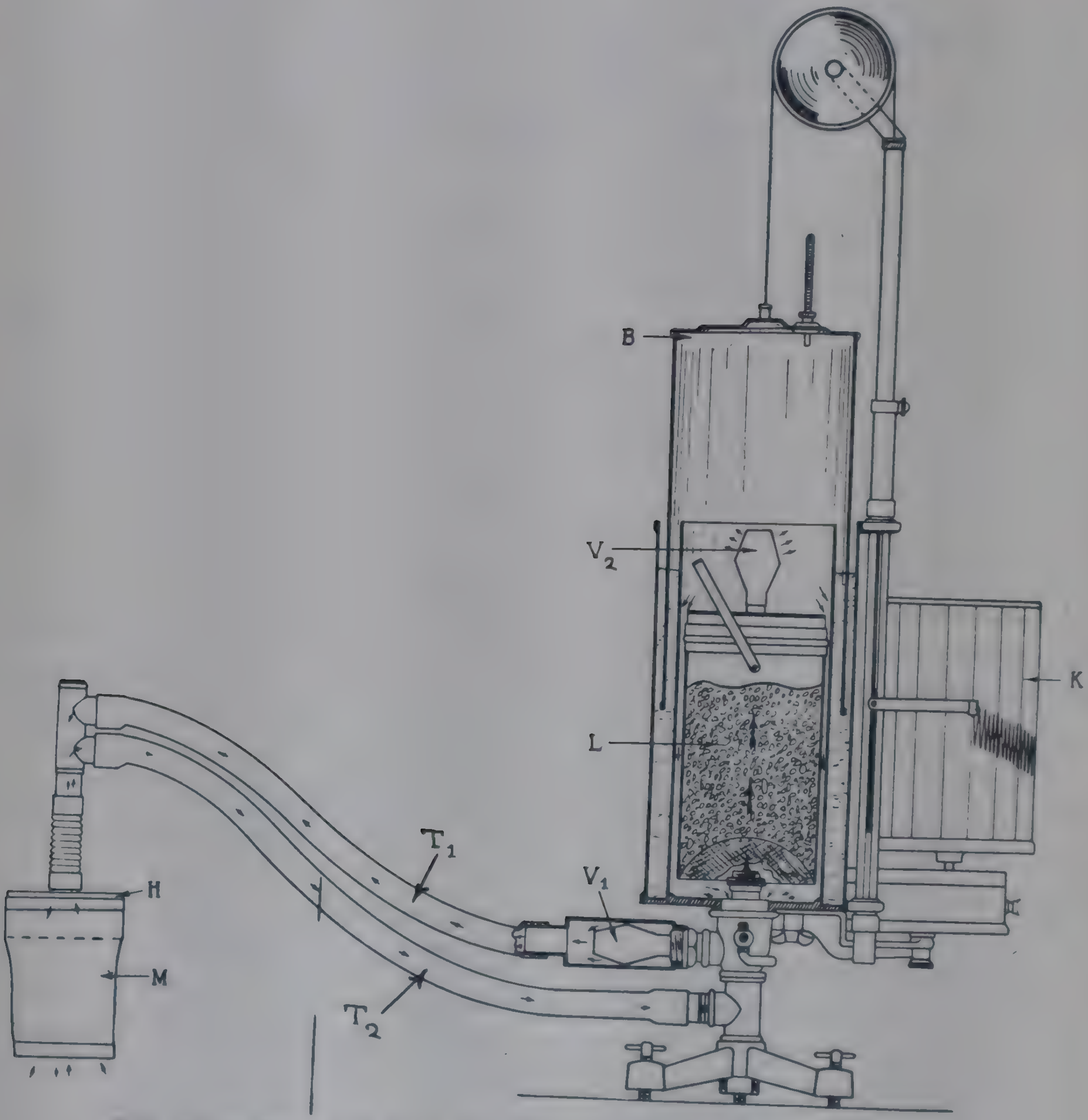

Fig. 12.1a—Benedict-Roth-Collins clinical metabolism apparatus.

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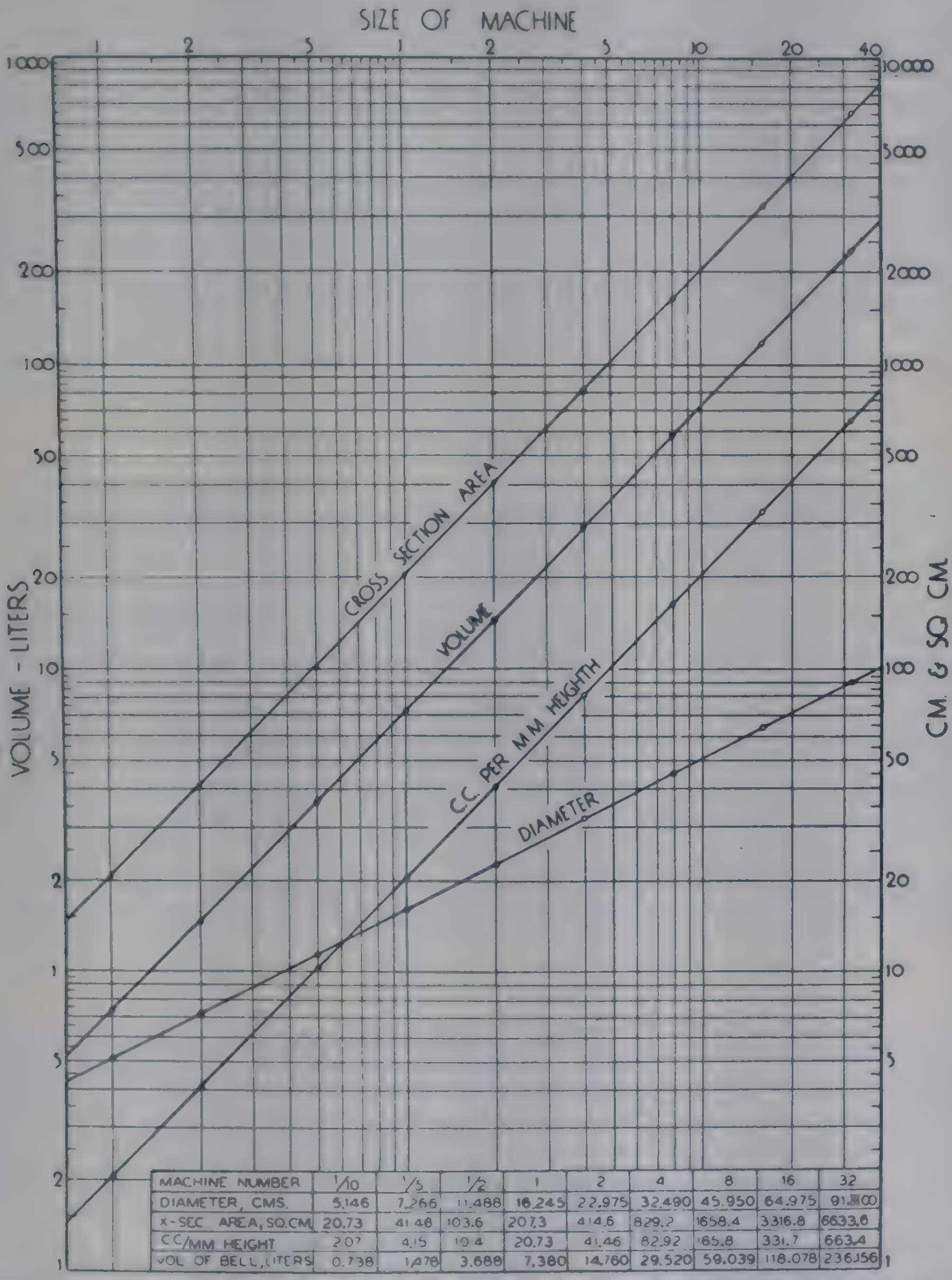
[15] Fredericq, L., *Arch. de Biol.*, **3**, 687 (1887); also in "Elements de physiologie humaine," 2nd ed., 1888, and in "Manipulations de Physiologie."

[16] Krogh, A., *Boston Med. and Surg. J.*, **189**, 313 (1923).

As previously noted, the advantage of using this graphic spirometer method for measuring ruminant metabolism is that the digestive-tract CO_2 exhaled by these animals is absorbed in soda lime (Fig. 12.1a) and is thus eliminated as a complicating factor.



MACHINE NUMBER	1/10	1/5	1/2	1	2	4	8	16	32
DIAMETER, CMS.	5.146	7.266	11.488	16.245	22.975	32.490	45.950	64.975	91.[illegible]00
X-SEC AREA, SQ.CM	20.73	41 46	103.6	207.3	414.6	829.2	1658.4	3316.8	6633.6
CC/MM HEIGHT	2.07	4.15	10.4	20.73	41.46	82.92	165.8	331.7	663.4
VOL OF BELL, LITERS	0.738	1.478	3.688	7.380	14.760	29.520	59.039	118.078	236.156

Fig. 12.1b—"We employed oxygen-bell sizes $\frac{1}{10}$, $\frac{1}{5}$, $\frac{1}{2}$, 1, 2, 4, 8, 16, and 32, depending on the size of the animal. Size 1 is that used in the standard Benedict-Roth apparatus (volume of 20.73 cc per mm height) and the others are multiples ($\frac{1}{10}$, $\frac{1}{5}$, etc.) of the #1 size. The given numerical values are here tabulated and plotted against the bell size on a logarithmic grid."

This method would indeed be ideal for ruminants except for the fact that they also exhale some CH_4 (after its absorption into the blood stream from the rumen[17]) which may accumulate in the oxygen bell, so that the decline

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[17] *Cf.* McIver, M. A., Redfield, A. C., and Benedict, E. B., "Gaseous exchange between blood and digestive tract," *Am. J. Physiol.*, **76**, 92 (1926).

TABLE 12.2.—Spirometers Classified by Machine Size.

Machine No.	Diameter (cm)	Cross-section area (sqcm)	CC/MM Height	Volume of bell (liters)	Cal to mm of Height
0.1	5.15	20.73	2.07	0.74	0.01
0.2	7.27	41.46	4.15	1.48	0.02
0.5	11.49	103.6	10.40	3.69	0.05
1	16.24	207.3	20.73	7.38	0.1
2	22.98	414.6	41.46	14.76	0.2
4	32.49	829.2	82.92	29.52	0.4
8	45.95	1658.4	165.8	59.04	0.8
16	64.98	3316.8	331.7	118.08	1.6
32	91.90	6633.6	663.4	236.16	3.2

Spirometers Classified by Diameters

Diameter (cm)	Cross-section area (sqcm)	CC/MMHeight	Diameter (cm)	Cross-section area (sqcm)	CC/MM Height
1	.785	.0785	48	1809.6	180.96
2	3.142	.3142	50	1963.5	196.35
3	7.069	.7069	52	2123.7	212.37
4	12.57	1.257	54	2290.2	229.02
5	19.64	1.964	56	2463.0	246.30
6	28.27	2.827	58	2642.1	264.21
7	38.49	3.849	60	2827.4	282.74
8	50.27	5.027	62	3019.1	301.91
9	63.62	6.362	64	3217.0	321.70
10	78.54	7.854	66	3421.2	342.12
12	113.1	11.31	68	3631.7	363.17
14	153.9	15.39	70	3848.5	384.85
16	201.1	20.11	72	4071.5	407.15
18	254.5	25.45	74	4300.8	430.08
20	314.2	31.42	76	4536.5	453.65
22	380.1	38.01	78	4778.4	477.84
24	452.4	45.24	80	5026.5	502.65
26	530.9	53.09	82	5281.0	528.10
28	615.8	61.58	84	5541.8	554.18
30	706.9	70.69	86	5808.8	580.88
32	804.3	80.43	88	6082.1	608.21
34	907.9	90.79	90	6361.7	636.17
36	1017.9	101.79	92	6647.6	664.76
38	1134.1	113.41	94	6939.8	693.98
40	1256.6	125.66	96	7238.2	723.82
42	1385.4	138.54	98	7543.0	754.30
44	1520.5	152.05	100	7854.0	785.40
46	1661.9	166.19	102	8171.3	817.13

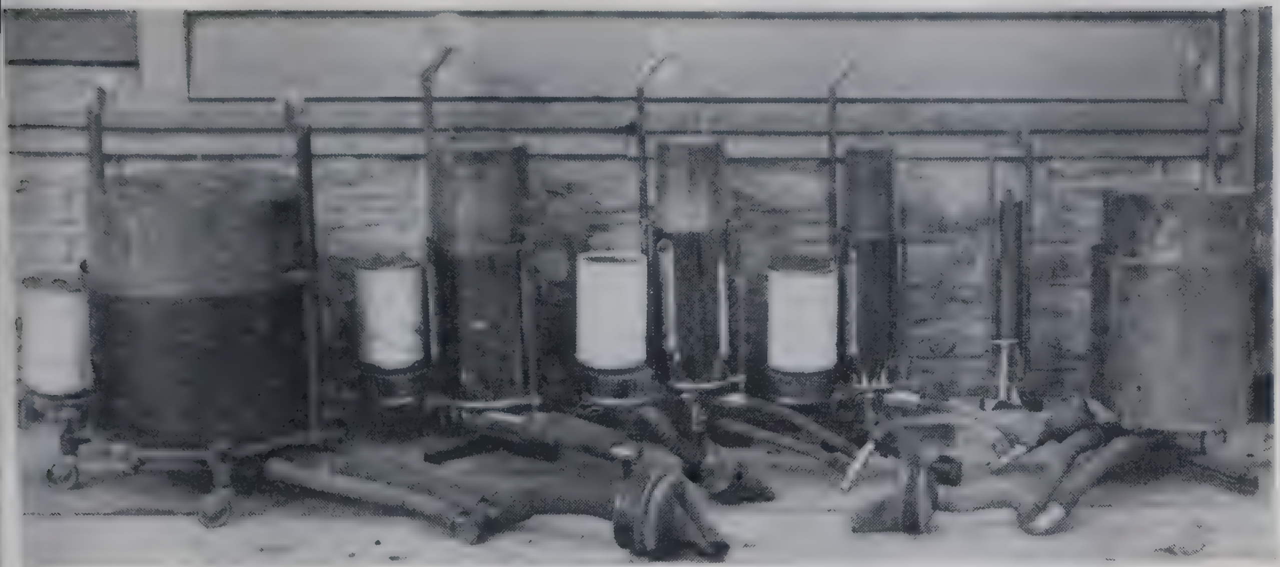

Fig. 12.2 The various designs and uses of the Benedict-Roth-Collins apparatus in our laboratory.

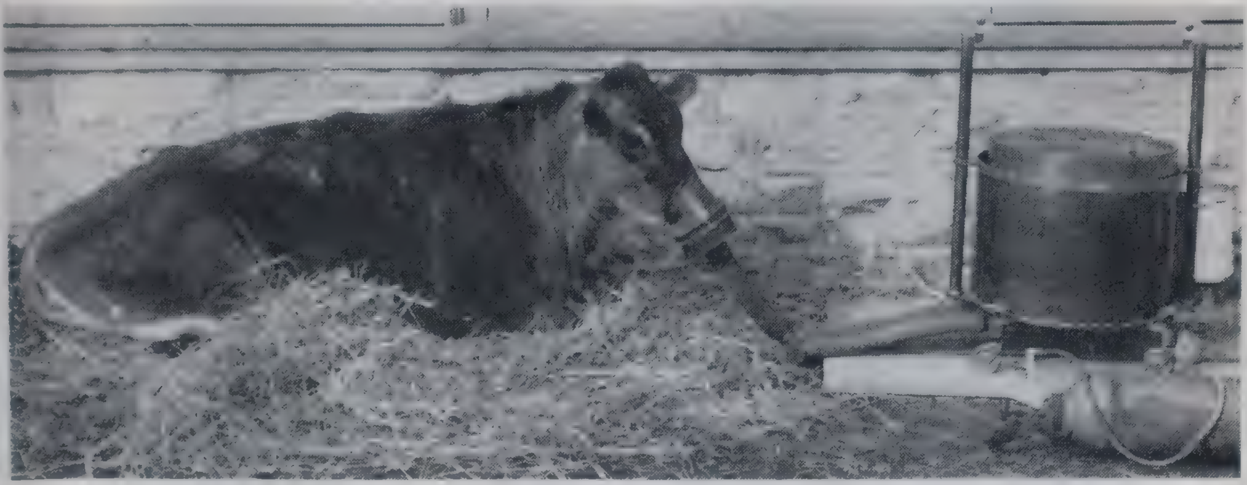

Fig. 12.3—See caption of 12.2.

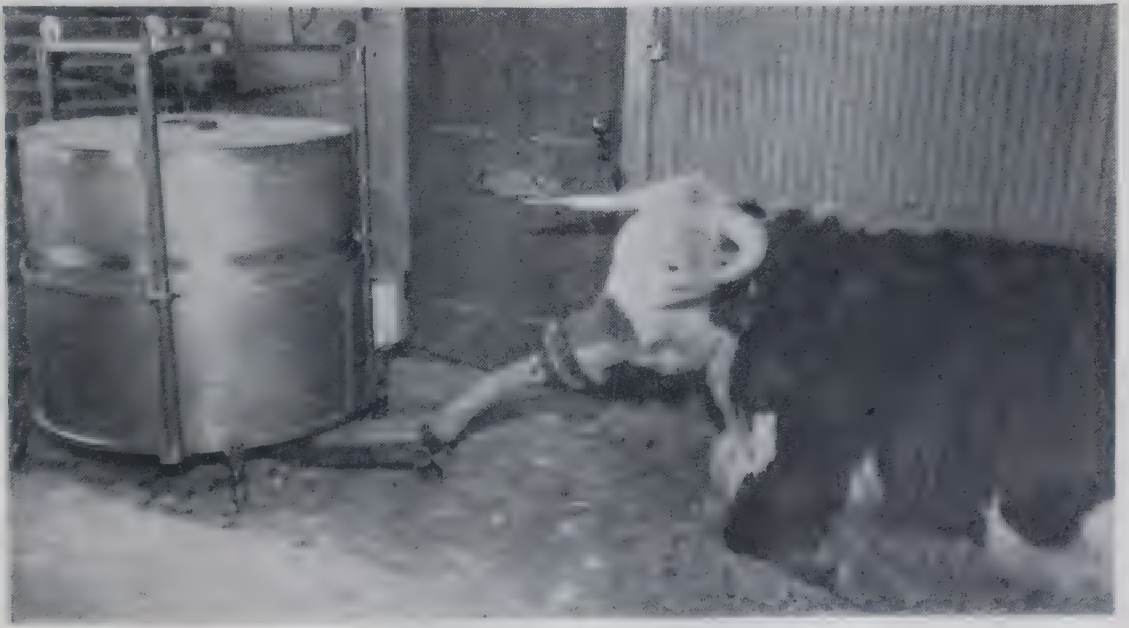

Fig. 12.4—See caption of 12.2.

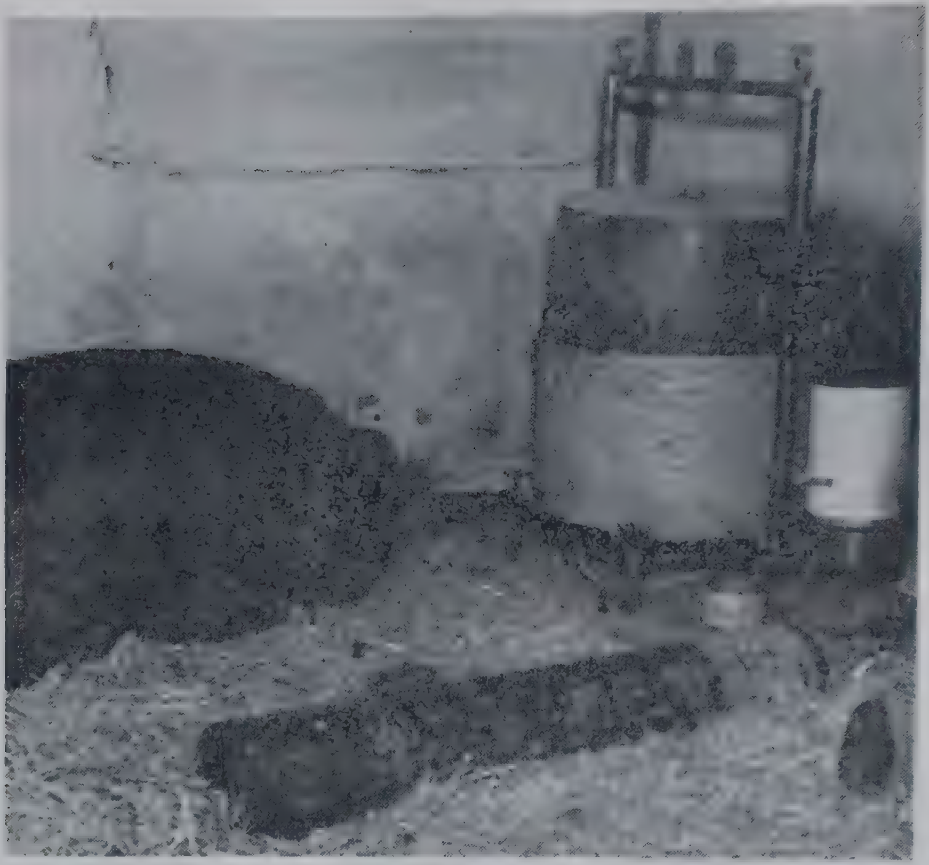

Fig. 12.5—See caption of 12.2.

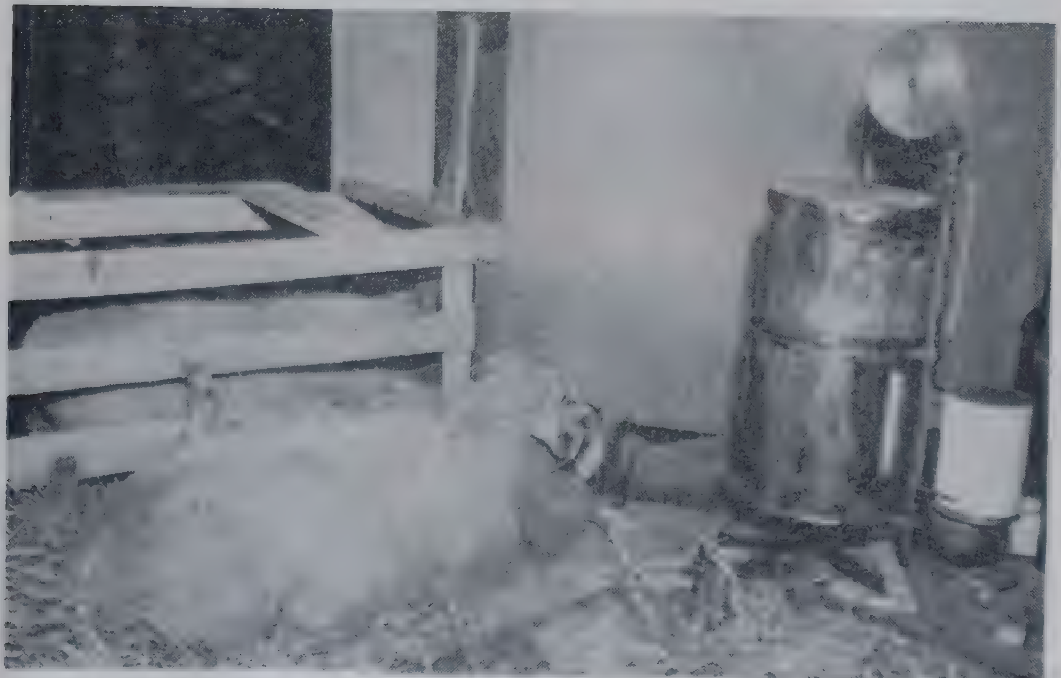

Fig. 12.6—See caption of 12.2

in the oxygen bell due to the consumption of its oxygen will be less by the volume of CH_4 accumulated. However, as shown in Fig. 12.9a, the error introduced thereby is relatively slight, perhaps 3 per cent, 8 to 12 hours after feeding. The oxygen consumption was measured regularly before the morning feeding. The graphic spirometer method, of course, involves only a part of the CH_4 eliminated, not that eliminated by rectum or regurgitated by the esophagus, because such more or less sudden gas elimination is graphically recorded, and the metabolism is measured by the smooth *slope* of the graphic record, not by the absolute change in height of the oxygen bell.

Fig. 12.8a presents observations on the relative heat production in goats obtained by the spirometer method which involves the CH_4 error (B) and by the open-circuit method which does not involve the CH_4 error (A); also by the spirometer method after correcting for CH_4 by analysis of the spirometer atmosphere for CH_4 (C, D).

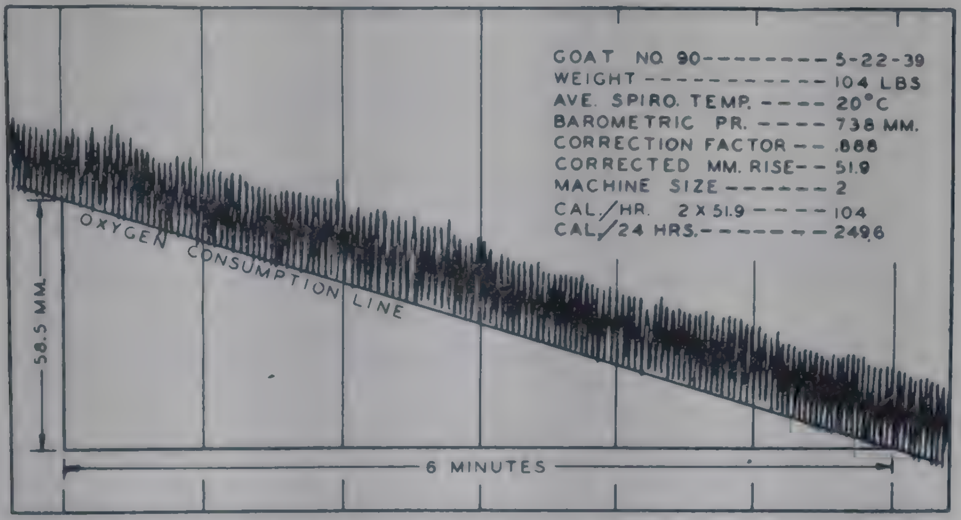

Fig. 12.7—A six-minute spirogram from which the rate of oxygen consumption is computed.

Fig. 12.8b presents data on methane production obtained by the spirometer open-circuit methods on both cows and goats; it demonstrates a very rapid decline in methane production following feeding. The methane error is inappreciable 48 hours after feeing; postabsorptive metabolism measured by the oxygen spirometer method does not suffer from the methane error.

12.2.2: Closed-circuit-chamber system for smaller animals[18]. As previously noted, the closed-circuit method was originated by Regnault and Reiset[19]. Fig. 12.10 represents the original Regnault-Reiset apparatus. The

(Text cont'd on p. 325)

[18] See Du Bois, E. F., "Metabolism in health and disease" for closed-circuit respiration chambers for humans.

[19] Regnault, V., and Reiset, J., "Récherches chimiques sur la respiration des animaux des diverses classes," *Ann. Chim. et de Physique*, **26**, 299 (1849).

TABLE 12.3.—Correction Factors* for Reducing Observed Volumes of Warm, 80% Saturated Air (or Oxygen) to Standard Conditions (Dry, 0°C, 760 mm)

$$\text{Formula } \frac{1}{1 + 0.00367t} + \frac{P - 0.80Pw\dagger}{760} = \text{Factor}$$

P (mm.)	Temperature °C																				
	15°	16°	17°	18°	19°	20°	21°	22°	23°	24°	25°	26°	27°	28°	29°	30°	31°	32°	33°	34°	35°
650	.798	.794	.791	.787	.784	.780	.777	.773	.769	.765	.761	.756	.752	.748	.744	.740	.736	.732	.727	.723	.619
655	.804	.800	.797	.793	.790	.786	.783	.779	.775	.771	.767	.762	.758	.754	.750	.746	.742	.738	.733	.729	.724
660	.810	.806	.803	.799	.796	.792	.789	.785	.781	.777	.773	.768	.764	.760	.756	.752	.748	.744	.739	.735	.730
665	.816	.812	.809	.805	.802	.798	.795	.791	.787	.783	.779	.774	.770	.766	.762	.758	.754	.749	.745	.741	.736
670	.822	.819	.816	.812	.809	.805	.801	.797	.793	.789	.785	.780	.776	.772	.768	.764	.760	.755	.751	.746	.742
675	.828	.825	.821	.818	.815	.812	.807	.803	.799	.795	.791	.786	.782	.778	.774	.770	.766	.761	.757	.752	.748
680	.834	.830	.827	.824	.821	.818	.813	.809	.805	.801	.797	.792	.788	.784	.780	.776	.771	.767	.763	.758	.754
685	.841	.837	.833	.830	.827	.824	.819	.815	.811	.807	.803	.798	.794	.790	.786	.782	.777	.773	.769	.764	.760
690	.848	.844	.841	.837	.833	.830	.825	.821	.817	.813	.809	.804	.800	.796	.792	.788	.783	.779	.775	.770	.765
695	.854	.850	.847	.843	.840	.836	.831	.827	.823	.819	.815	.810	.806	.802	.798	.794	.789	.785	.780	.776	.771
700	.860	.856	.853	.849	.846	.842	.837	.833	.829	.825	.821	.816	.812	.808	.804	.800	.795	.791	.786	.781	.777
705	.866	.862	.859	.855	.852	.848	.843	.839	.835	.831	.827	.822	.818	.814	.810	.806	.801	.796	.792	.787	.783
710	.872	.868	.865	.861	.858	.854	.849	.845	.841	.837	.833	.828	.824	.820	.816	.812	.807	.802	.798	.793	.788
715	.878	.874	.871	.867	.864	.860	.855	.851	.847	.843	.839	.834	.830	.826	.822	.818	.813	.808	.804	.799	.794
720	.885	.881	.877	.873	.870	.866	.861	.857	.853	.849	.845	.840	.836	.832	.828	.824	.819	.814	.810	.805	.800
725	.891	.887	.883	.879	.876	.872	.867	.863	.859	.855	.851	.846	.842	.838	.834	.830	.825	.820	.816	.811	.806
730	.897	.894	.890	.886	.882	.878	.873	.869	.865	.861	.857	.852	.848	.844	.840	.836	.831	.826	.822	.817	.812
735	.904	.900	.896	.892	.888	.884	.879	.875	.871	.867	.863	.858	.854	.850	.846	.842	.837	.832	.827	.822	.817
740	.910	.906	.902	.898	.894	.890	.885	.881	.877	.873	.869	.864	.860	.856	.852	.848	.843	.838	.833	.828	.823
745	.916	.912	.908	.904	.900	.896	.891	.887	.883	.879	.875	.869	.865	.861	.857	.853	.848	.844	.839	.833	.828
750	.922	.918	.914	.910	.906	.902	.897	.893	.889	.885	.881	.875	.871	.867	.863	.859	.854	.849	.845	.840	.835
755	.928	.924	.920	.916	.912	.908	.903	.899	.895	.891	.887	.881	.877	.873	.869	.865	.860	.855	.851	.846	.841
760	.934	.930	.926	.922	.918	.914	.909	.905	.901	.897	.893	.887	.883	.879	.875	.871	.866	.861	.857	.852	.847
765	.941	.936	.932	.928	.924	.920	.915	.911	.907	.903	.899	.893	.889	.885	.881	.877	.872	.867	.863	.857	.852
770	.947	.943	.939	.935	.930	.926	.921	.917	.913	.909	.905	.899	.895	.891	.887	.883	.878	.873	.869	.863	.850
775	.954	.949	.945	.941	.936	.932	.927	.923	.919	.915	.911	.905	.901	.897	.893	.889	.884	.879	.875	.869	.864
780	.960	.956	.952	.948	.943	.939	.934	.930	.926	.921	.917	.911	.907	.903	.899	.895	.890	.885	.880	.875	.870

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[*] Table calculated by Tyler Fuwa on basis of table by E. H. Clarke. The above table is reprinted from Professor Robert E. Wilson's paper on "The Moisture Absorbing Efficiency of Carbon Dioxide Absorbents for Metabolism Apparatus", *Boston Medical & Surgical J.*, **187**, 133 (1922) and *J. Ind. Eng. Chem.*, **12**, 1000 (1920). The correction factors are intended, and are accurate only, for metabolism apparatus filled with a high moisture (15–19%), low alkali (5%) CO_2-absorbent soda lime, such as Wilson Soda Lime. The Wilson soda lime employed for absorbing CO_2 in metabolism apparatus maintains a relative humidity of 80 per cent throughout the apparatus and never above 90 per cent.

TABLE 12.3A.—Values Extrapolated from Table 12.3.

P (mm)	Temperature °C																			
	−4°	−3°	−2°	−1°	0°	1°	2°	3°	4°	5°	6°	7°	8°	9°	10°	11°	12°	13°	14°	15°
740	.985	.981	.977	.973	.969	.965	.961	.957	.953	.949	.945	.942	.938	.934	.930	.926	.922	.918	.914	.910
741	.986	.982	.978	.974	.970	.966	.962	.958	.954	.950	.947	.943	.939	.935	.931	.927	.923	.919	.915	.911
742	.987	.983	.979	.975	.971	.967	.963	.959	.955	.952	.948	.944	.940	.936	.932	.928	.924	.920	.916	.912
743	.989	.985	.981	.977	.973	.969	.965	.961	.958	.954	.950	.946	.942	.938	.934	.930	.926	.922	.918	.914
744	.990	.986	.982	.978	.974	.970	.967	.963	.959	.955	.951	.947	.943	.939	.935	.931	.927	.923	.919	.915
745	.991	.987	.983	.979	.975	.972	.968	.964	.960	.956	.952	.948	.944	.940	.936	.932	.928	.924	.920	.916
746	.993	.989	.985	.981	.977	.973	.969	.965	.961	.957	.953	.949	.945	.941	.937	.933	.929	.925	.921	.917
747	.994	.990	.986	.982	.978	.974	.970	.966	.962	.958	.954	.950	.946	.942	.938	.934	.930	.926	.922	.918
748	.996	.992	.988	.984	.980	.976	.972	.968	.964	.960	.956	.952	.948	.944	.940	.936	.932	.927	.924	.920
749	.997	.993	.989	.985	.981	.977	.973	.969	.965	.961	.957	.953	.949	.945	.941	.937	.933	.929	.925	.921
750	.998	.994	.990	.986	.982	.978	.974	.970	.966	.962	.958	.954	.950	.946	.942	.938	.934	.930	.926	.922
751	.999	.995	.991	.987	.983	.979	.975	.971	.967	.963	.959	.955	.951	.947	.943	.939	.935	.931	.927	.923
752	1.000	.996	.992	.988	.984	.980	.976	.972	.968	.964	.960	.956	.952	.948	.944	.940	.936	.932	.928	.924
753	1.002	.998	.994	.990	.986	.982	.978	.974	.970	.966	.962	.958	.954	.950	.946	.942	.938	.934	.930	.926
754	1.003	.999	.995	.991	.987	.983	.979	.975	.971	.967	.963	.959	.955	.951	.947	.943	.939	.935	.931	.927
755	1.005	1.001	.997	.993	.989	.985	.981	.977	.973	.969	.965	.961	.957	.953	.949	.945	.941	.937	.933	.928

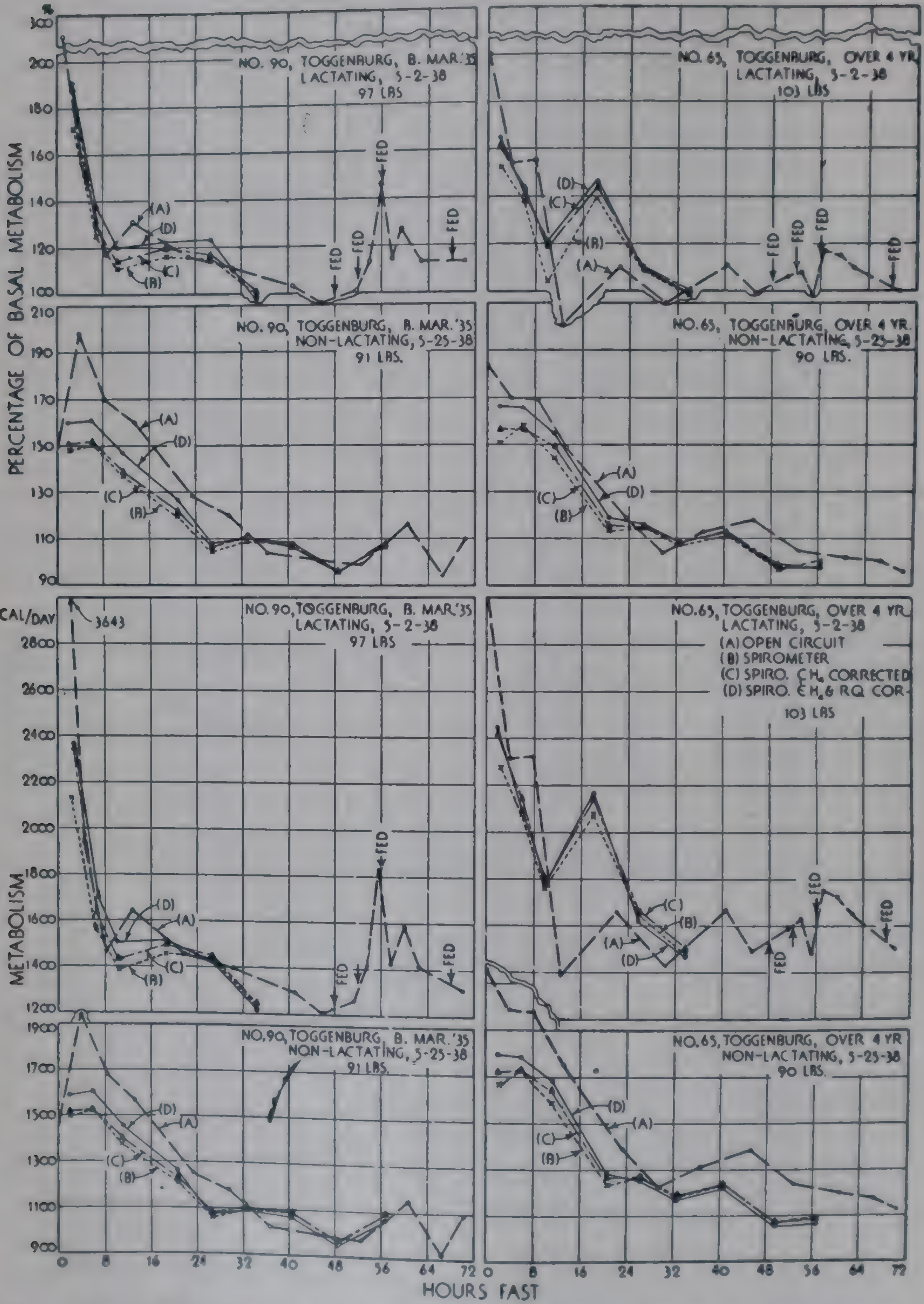

Fig. 12.8a—The decline in apparent heat production with time after feeding in goats determined by: (A) open circuit method corrected for CH_4; (B) spirometer method not corrected for CH_4; (C) spirometer method corrected for CH_4 by analyzing residual air in the spirometer; (D) spirometer method corrected for CH_4 *and* changes in the R. Q. determined for alternate 30-minute periods by open-circuit method.

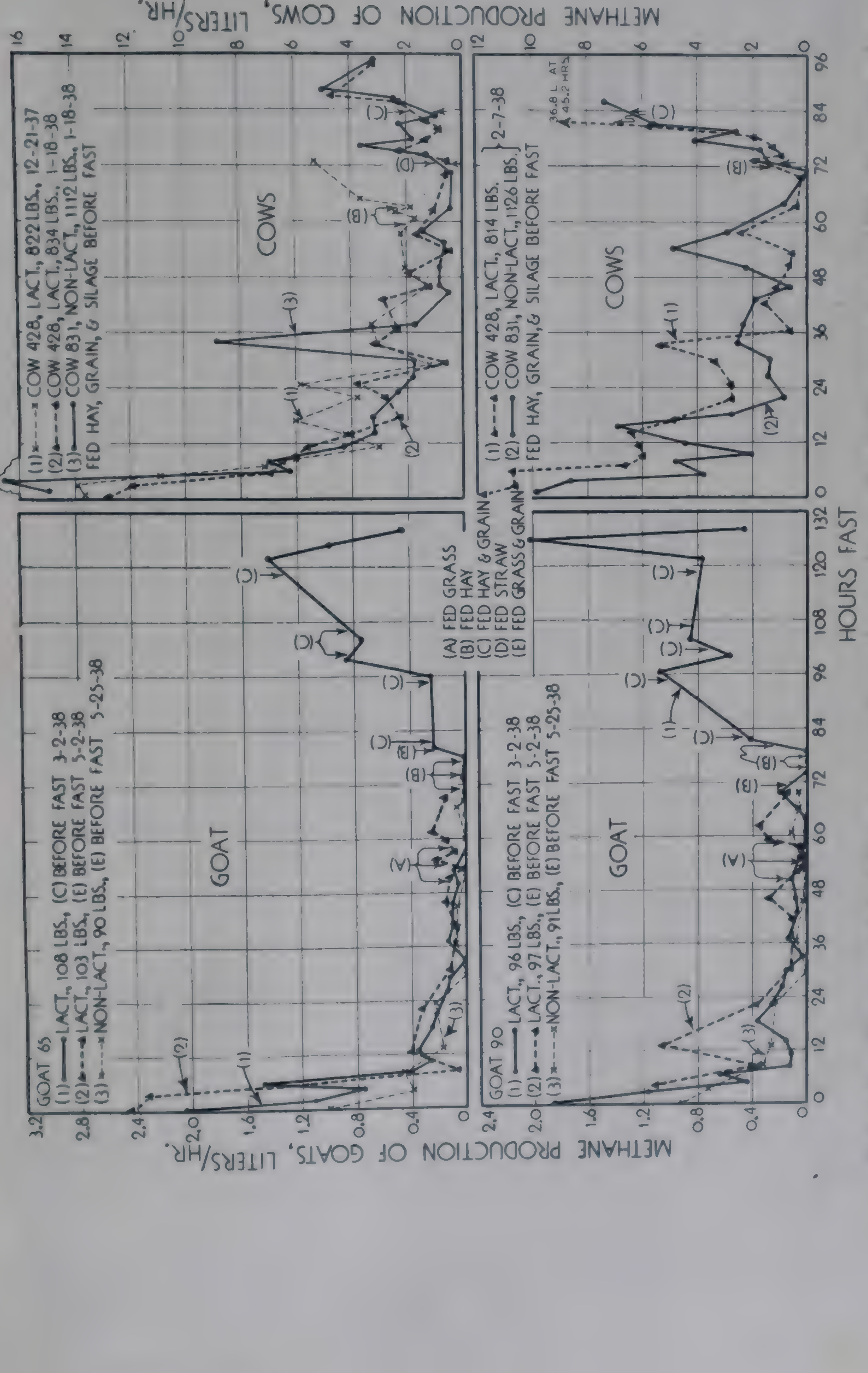

Fig. 12.8b—Time curves of CH_4 production during fast and refeeding to illustrate the rapidity of decline of methane production with time after feeding.

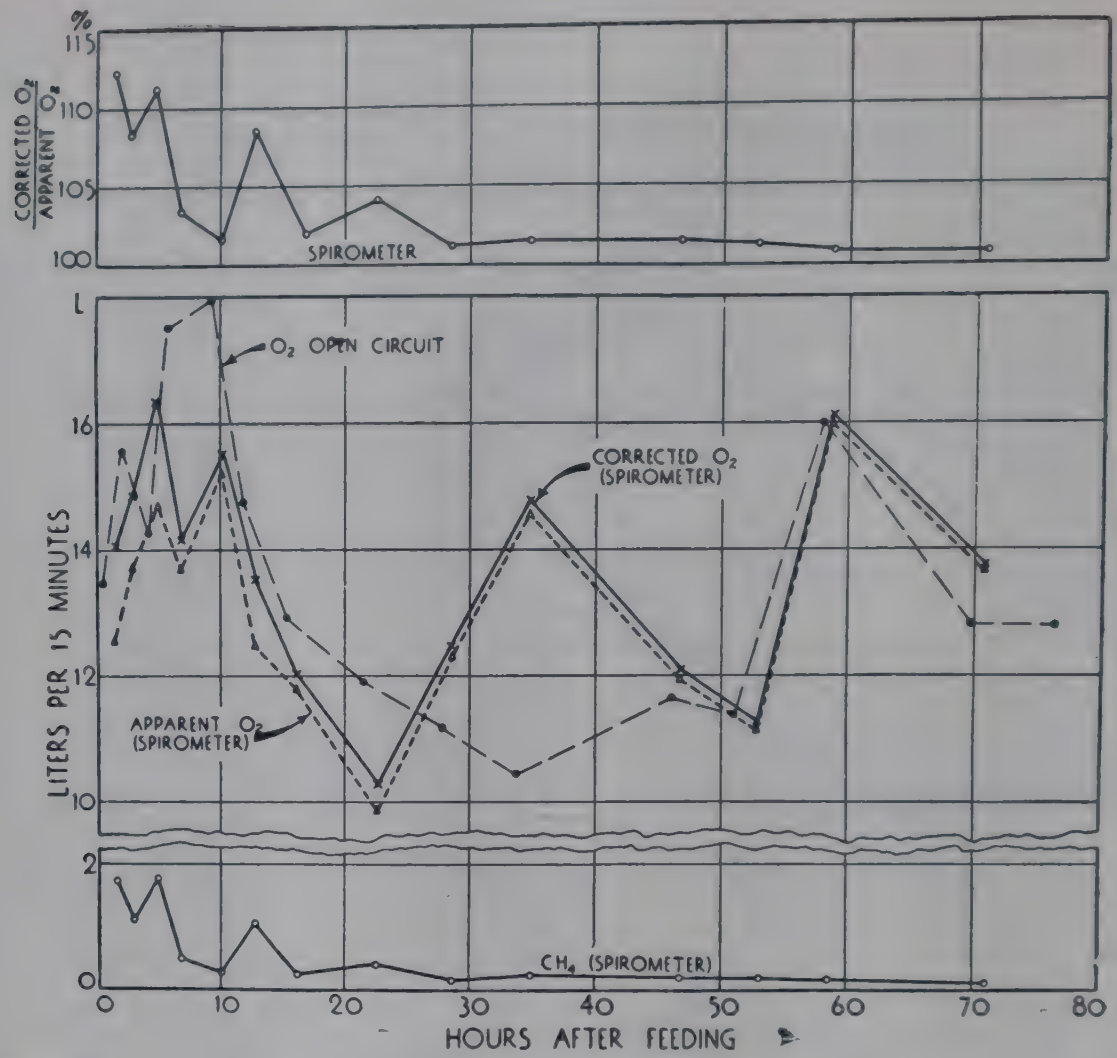

Fig. 12.9a—Comparison of apparent rates of O_2 consumption by spirometer and open-circuit methods in cows.

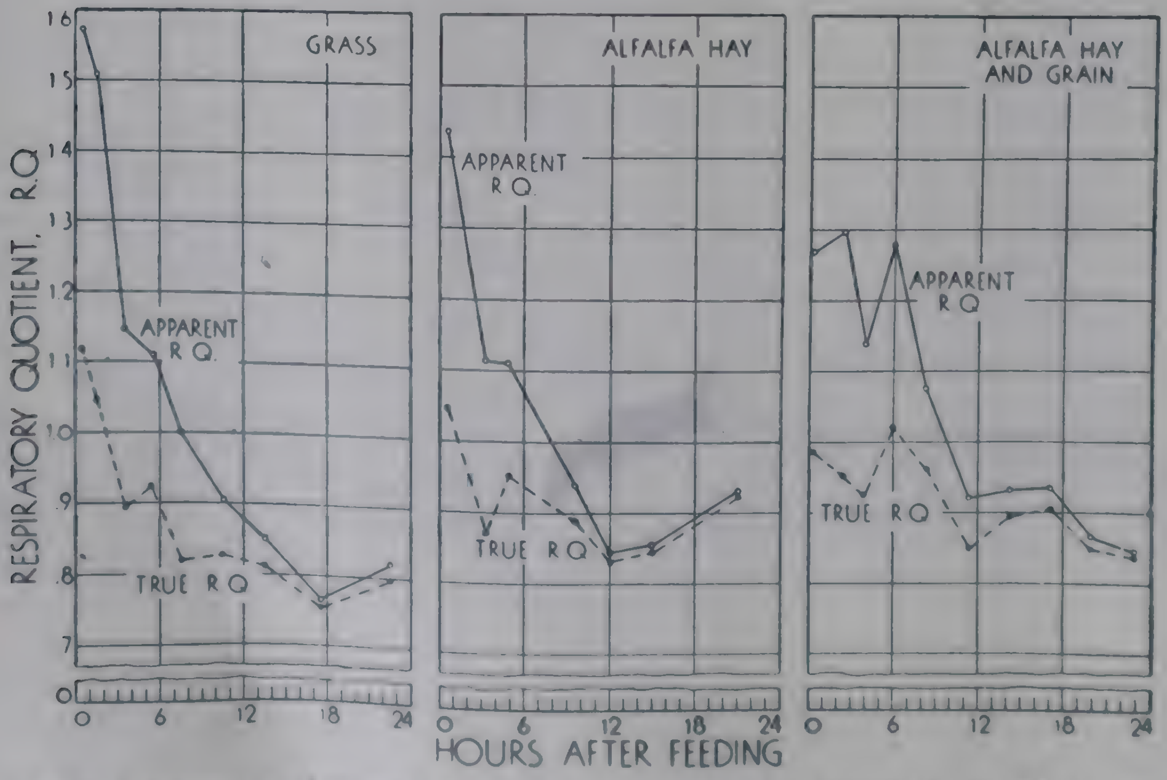

Fig. 12.9b—Apparent and "true" R. Q. after corrected for fermentation CO_2 in cows.

writer has seen a modification of it used by Professor Otto Kestner in Hamburg. In this country Kleiber[20] uses a modification for measuring the metabolism of rats, and Winchester[21] for chickens. We[22] employed similar apparatus for small laboratory animals from mice to chickens. The following description is for Winchester's apparatus constructed in the writer's labaratory for the domestic fowl. One of the four independent respiration chambers is illustrated in Fig. 12.11a. Fig. 12.11b is a photograph of both our large (fowl) and small (rat) apparatus. At least the Mariotte bottles show clearly.

This apparatus consists of 4 parts: (1) constant-temperature cabinet; (2) burette system (8-liter capacity) consisting of three tubes (110 cm long), two large (7 cm in diameter) and one ordinary titration burette, 1 cm in diameter, all interconnected so that they have the same water level (1.0 cc in the burette corresponds to 74 cc in the entire burette system composed of the three tubes); (3) Mariotte bottle; (4) CO_2 absorbers. There are also auxiliary items, including pressure gauge; equilibrator, which adjusts temperature of water in Mariotte bottle to that of chamber, and O_2 concentration of the water to that prevailing at chamber temperature; O_2 spirometer, which keeps air out of the top of the Mariotte bottle by connection with pure O_2; rocking mechanisms; fans; and so on.

Because of the sensitiveness of gas volume to temperature change, the apparatus is kept in a constant-temperature cabinet. Four 100-watt electric lamps, which are connected to a relay switch controlled by a mercury-acetone thermo-regulator, together with two 10-inch fans, keep the cabinet (194 × 43 × 122 cm) temperature constant (at 30° C) within 0.1° C.

The rate of O_2 consumption is measured by the rise of the water in the burette. As the O_2 from the burette system is consumed, it is replaced by water which automatically flows from the Mariotte bottle whenever the pressure at the siphon tube outlet falls below that at the inlet. (In the Mariotte bottle the bottom of the O_2 inlet is at such a level that the pressure of H_2O above it plus the pressure of the air above the water level is equal to the pressure at the siphon tube outlet.)

The CO_2 is absorbed in the battery by a saturated $Ba(OH)_2$ solution, prepared by mixing 100 cc each of $2N$ KOH and molal $BaCl_2$. The $Ba(OH)_2$-solution battery consists of 2 sets of two flat-bottomed flasks (each 500 cc for chickens) joined near the bottom by a glass tube. The alkaline solution flows from one flask to the other, alternately drawing air from and returning it to the chamber (at the rate of 12 liters per minute).

The rate of O_2 consumption is easily and accurately measured by the rise of water in the burette. The CO_2 production is determined by titration of the standardized alkaline CO_2-absorbing solution. The R.Q. is computed from the CO_2 and O_2 values.

If the R.Q. is not needed, the rate of O_2 consumption is measured by reading the burette at 10-minute intervals until several successive readings check. In this manner the metabolism may be estimated in 1 to 1½ hours instead of the 2 to 4 hours required when the R.Q. is determined.

The O_2-consumption measurements do not begin until after the animal has been in the chamber for ½ hour, in order to (1) accustom the animal to the chamber, (2) bring the system to the standard temperature (30° C), (3) establish an equilibrium between the

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[20] Kleiber, M., "A respiration apparatus for serial work with small animals, particularly rats," *Univ. Calif. Publ. Physiol.*, **8**, 207 (1940).

[21] Winchester, C. F., "Seasonal metabolic and endocrine rhythms in the domestic fowl," Univ. Missouri Agr. Exp. Sta. Res. Bull., 315, 1940.

[22] Kibler, H. H., and Brody, S., "Metabolism and growth rate of rats," *J. Nut.*, **24**, 461 (1942).

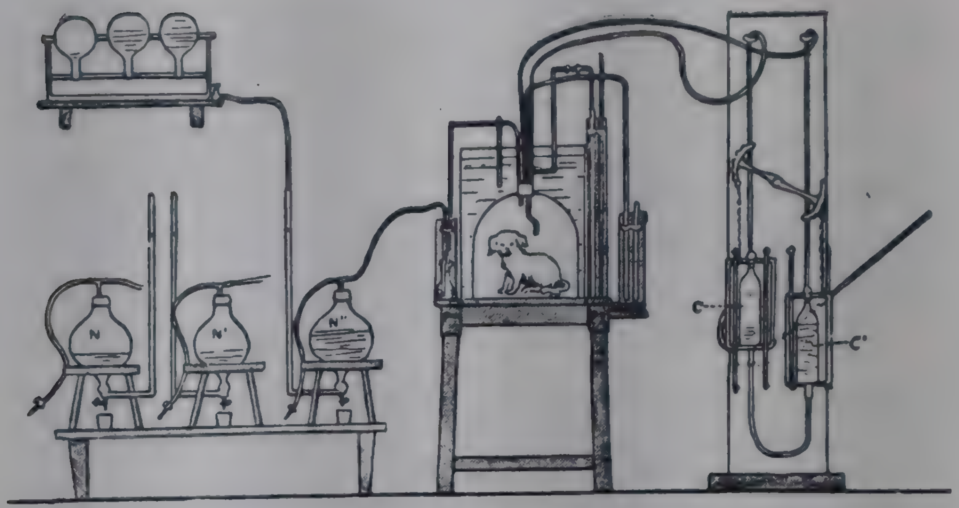

Fig. 12.10—The original Regnault-Reiset metabolism apparatus.

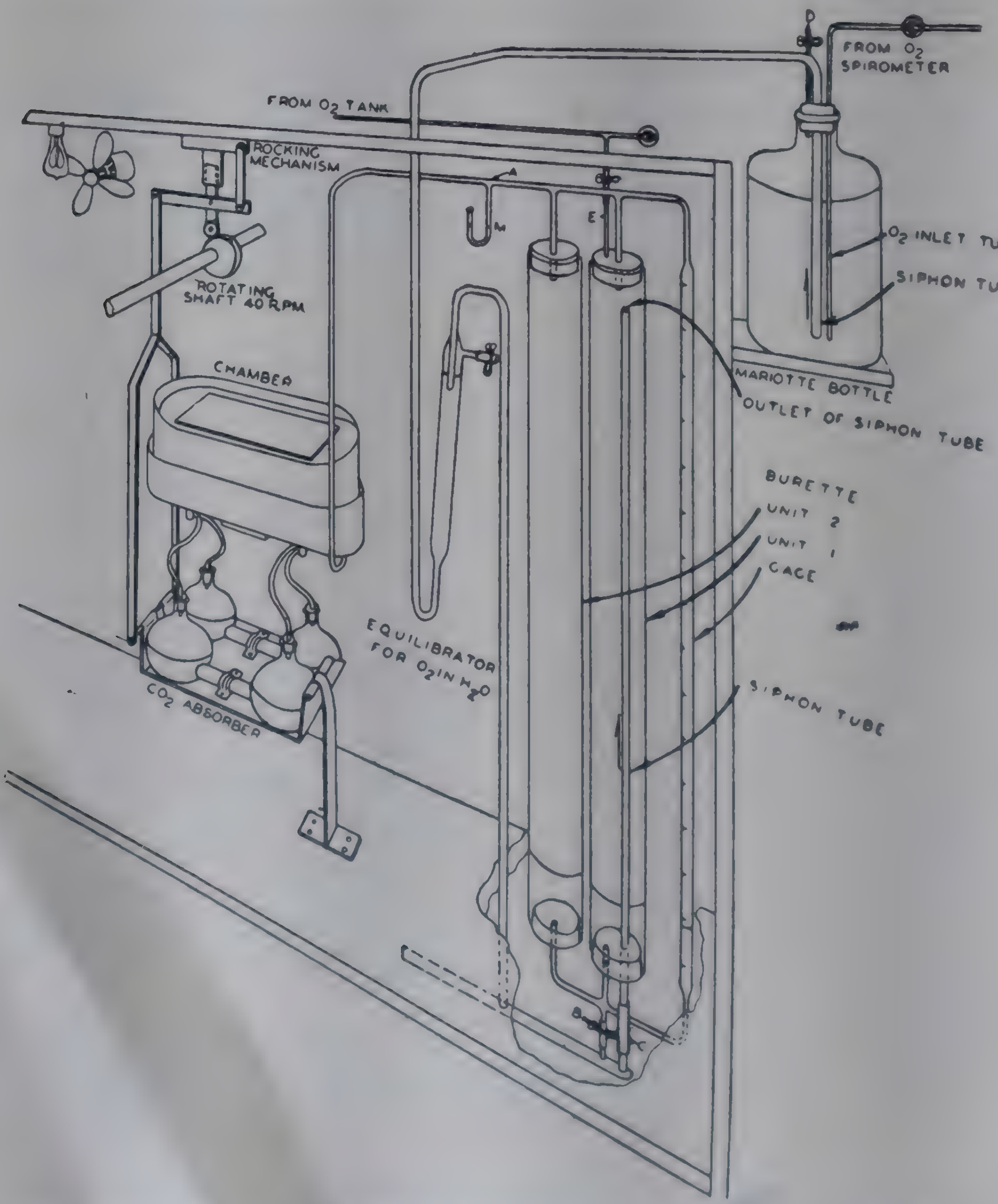

Fig. 12.11a—A unit of the 4-chamber Regnault-Reiset apparatus as used by Winchester in our laboratory for measuring the metabolism of chickens.

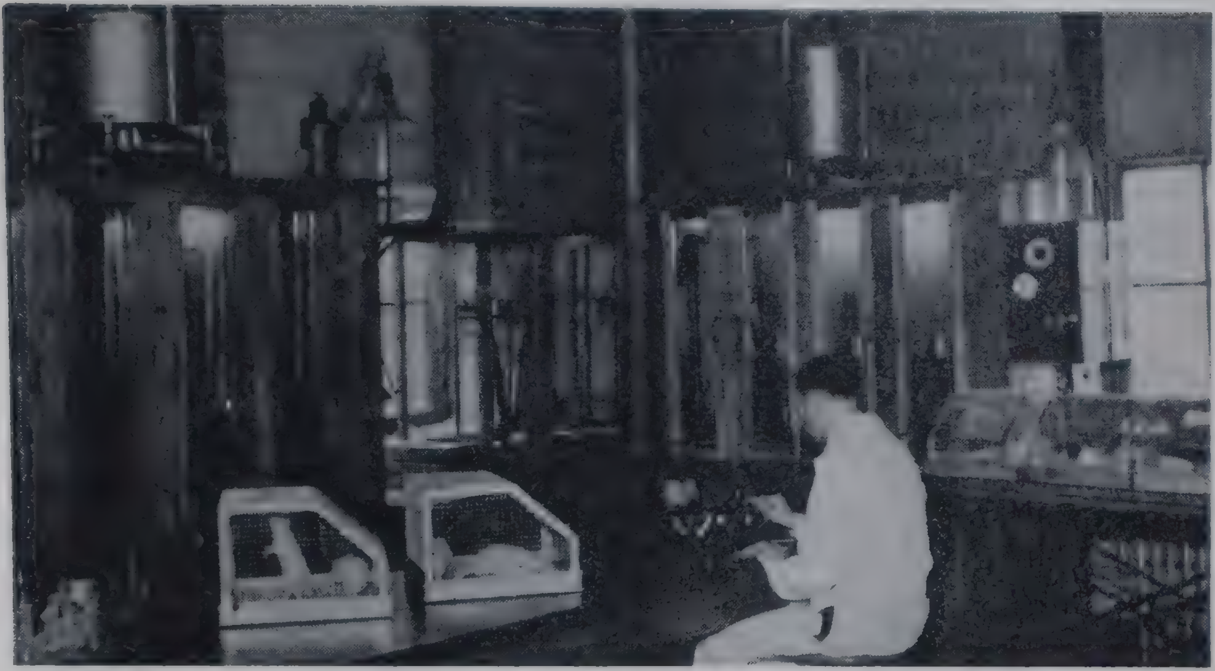

Fig. 12.11b—Regnault-Reiset apparatus, right 8-chamber apparatus for rats, left 4-chamber apparatus for chickens, and rabbits.

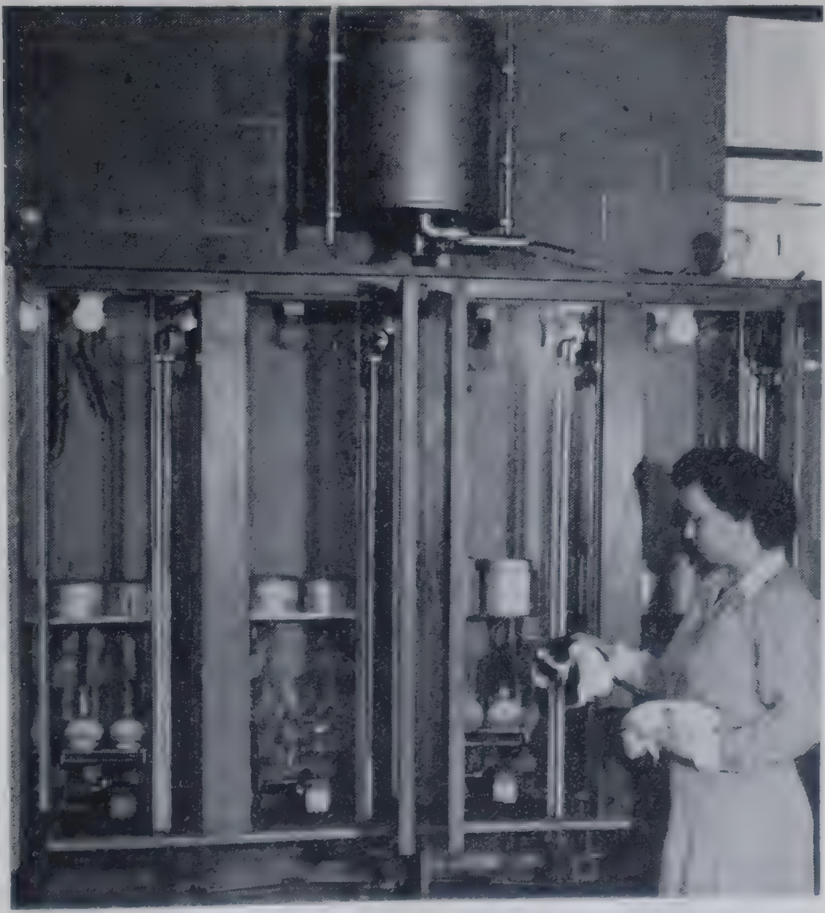

Fig. 12.11c—Regnault-Reiset apparatus.

absorbing rate of the battery and the CO_2-production rate. (The chamber air contains about 1 per cent CO_2 at the end of the first half, and this concentration remains approximately constant throughout the trial.)

Our rat-apparatus burette system has an O_2 capacity of 1 lit (1 cc in the graduate burette corresponds to 10 cc in the system; length of the burette, 106 cm). The chamber volumes are 1.0 to 1.2 liters. The temperature is controlled by 150-watt chromnickel resistance coils (instead of light bulbs.)

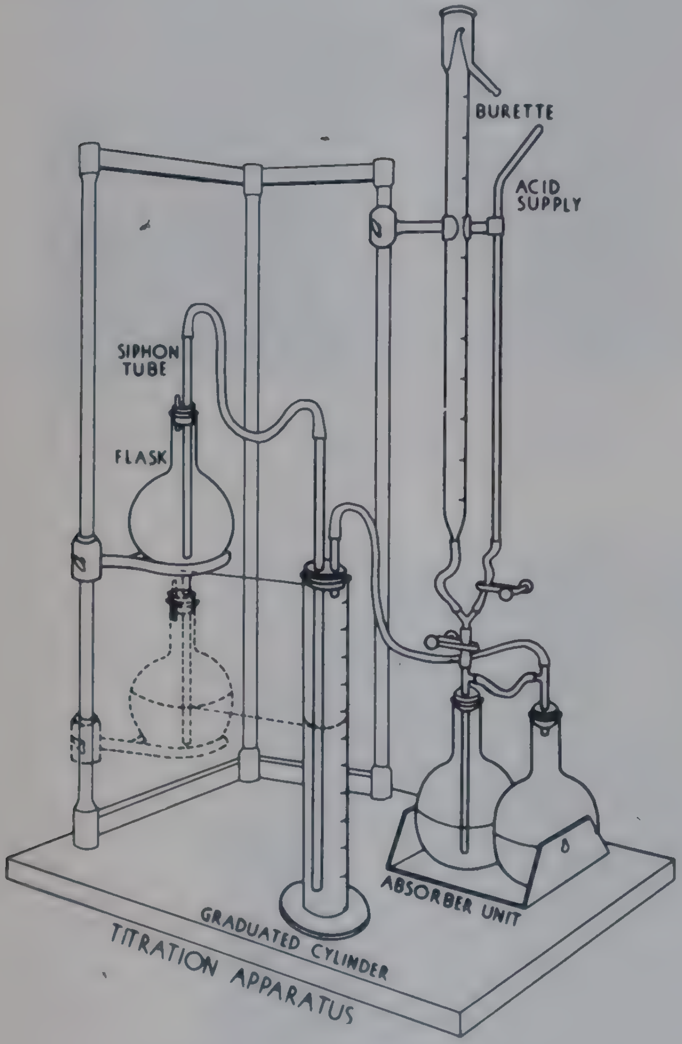

Fig. 12.12—Titration arrangement for the Regnault-Reiset apparatus.

The titration apparatus illustrated in Fig. 12.12 prevents CO_2 loss during titration, as any CO_2 lost from the absorber solution is held in the cylinder where it can be measured. The titrating acid is liberated below the surface of the alkaline-absorber solution. A thymol blue-cresol red solution affords a sharp color change from purple to orange-yellow at the end point.

Computation example: A fowl was placed in a chamber at 7 p.m. and the first oxygen reading was made half an hour later. In the following example only the initial and end readings are given.

Volume of chamber air + tubes and absorbers	7.00 liters
Volume of bird (the figure for weight in kilograms is taken to represent volume of the animal)	1.73 "
Chamber + tubes and absorbers + volume of animal	5.27 "

Oxygen Consumption

1 Time	2 Burette Reading	3 Volume of gas in burette	4 Burette Vol. + air in the chamber, absorber, etc.	5 Temperature (°C)	6 Barometric Pressure	7 Factor for Volume	8 Volume (Standard)	9 Volume (Difference)
7:30	93.1	7.26	12.53	30.0	74.7	.847	10.61	
10:00	52.0	4.31	9.58	30.0	74.7	.847	8.11	2.50
O_2 consumed		2.95	2.95					

O_2 consumed (corrected) = 2.50 liters (2.95 × .847) 2.50

O_2 consumed in 2.5 hours	2.50 liters
O_2 consumed in 1.0 hour	1.00 liter

CO_2 Production

KOH solution in battery	200	cc
$BaCl_2$ solution in battery	200	cc
This was found to be equivalent to	166.5	cc of 2.11*N* HCl
HCl used in titration	68.7	cc of 2.11*N* HCl
CO_2 absorbed equivalent to	97.8	cc of 2.11*N* HCl
1 cc. of 2.11 N HCl is equivalent to	23.63	cc of CO_2
In 3 hours CO_2 production was	2311.0	cc of CO_2
In 1 hour CO_2 production was	770.3	cc of CO_2 or 0.77 liter

$$\text{R.Q.} = \frac{CO_2/\text{hr}}{O_2/\text{hr}} = \frac{0.77}{1.00} = 0.77$$

Heat Production

For R.Q. 0.77, a liter of O_2 is equivalent to 4.8 Cal = 4.8 Cal/hour
Body weight of the fowl = 1.729 kg = 1.48 $\text{kg}^{0.73}$

Possible objections to this Regnault-Reiset method are: (1) it does not permit measurement of the water vaporization, as is possible by the Haldane gravimetric method which will be described presently; (2) the atmosphere is saturated with moisture which, at higher environmental temperatures, tends to depress the heat regulation of the body by water vaporization.

12.2.3: Open-circuit gravimetric method for smaller animals. This method, devised by Haldane[23], is the easiest to set up and to maintain, and also to operate, especially if the R.Q. is not needed. Depending on available size of scales, it may be used for animals ranging in weight from mice to large rabbits. We used it for fowl[24] (Fig. 12.15), rabbits, and rats[25] (Figs. 12.16 and 12.17).

The principle may be explained by referring to the original Haldane design, Fig. 12.14. This consists of a respiration chamber, *Ch*, which may be an ordinary fruit jar, in which the animal is kept, and several H_2O and CO_2 absorbers. The H_2O is usually absorbed by concentrated H_2SO_4 (in which lumps of pumice stone may be placed for increased area) or by such dry H_2O absorbers as magnesium perchlorate. The CO_2 is absorbed by alkali, such as a concentrated solution of NaOH or $Ba(OH)_2$, or more conveniently by "shell caustic". Soda lime is less convenient.

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[23] Haldane, J. S., *J. Physiol.*, **13**, 419 (1892).

[24] Phillips, V. W., Ashworth, U. S., and Brody, S., Univ. Missouri Agr. Exp. Sta. Res. Bull. 179, 1932.

[25] Herring, V., and Brody, S., *Id.* Res. Bull., 274, 1938. Brody and Nisbet, R., *Id.* Res. Bull., 285, 1938.

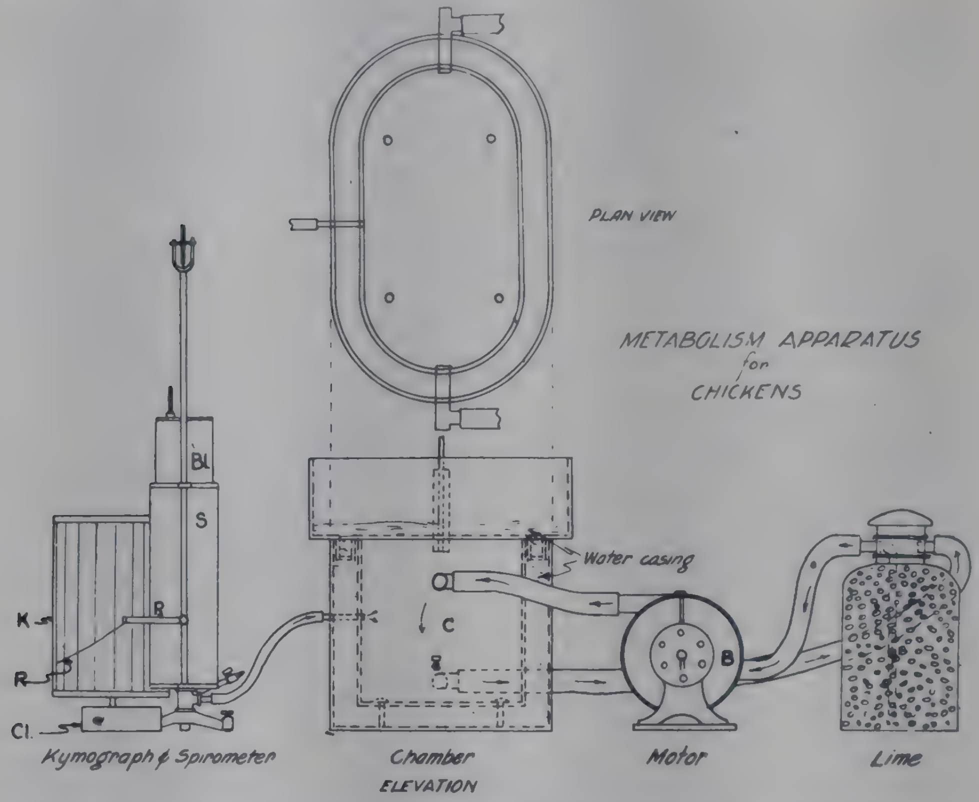

Fig. 12.13a—A closed circuit apparatus for measuring the O_2 consumption by the spirometer method.

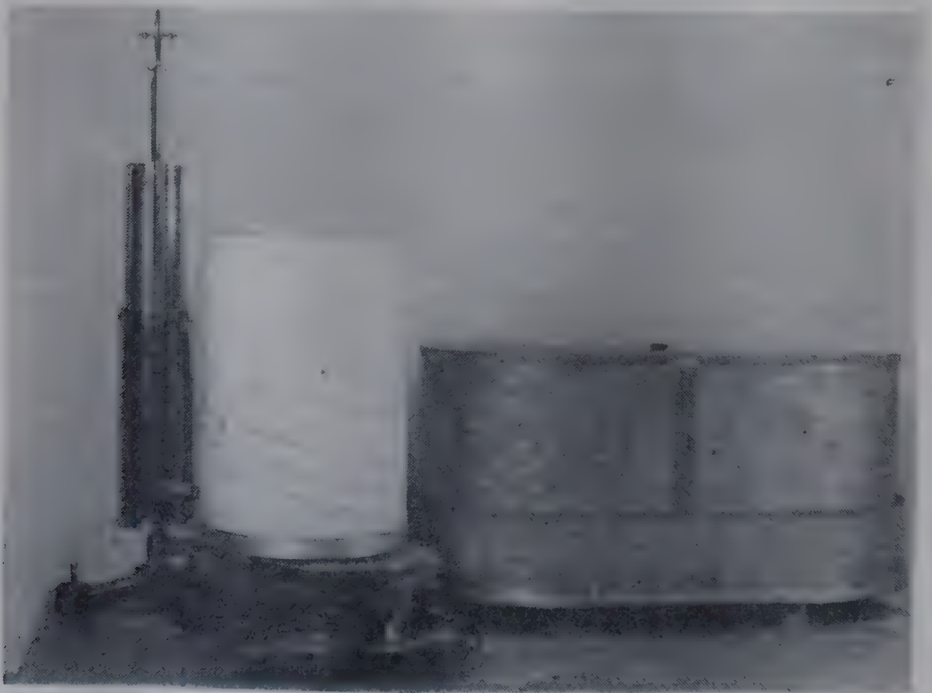

Fig. 12.13b—A closed circuit apparatus for measuring the O_2 consumption by the spirometer method.

Air is drawn through the chamber and absorbers by some pump, such as a water pump, *P*. It is convenient to keep a record of the rate of air passage by some meter, *M*.

The air is freed from its CO_2 and H_2O by absorbers 1 and 2, respectively, before it enters the chamber, *Ch*; the air leaving the chamber deposits its H_2O and CO_2 in absorbers 3 and (4 + 5) respectively. Thus some atmospheric O_2 is retained by the system (in the form of CO_2), but nothing leaves the system. Hence, while the *animal loses weight* during the trial (it loses H_2O and CO_2), the *system as a whole* (that is chamber and absorbers 3, 4, 5) *gains weight*; the gain represents O_2 consumed. So, we have H_2O vaporized (absorber 3); CO_2 produced (absorbers 4 and 5); and O_2 consumed (gain in the system *as a whole*).

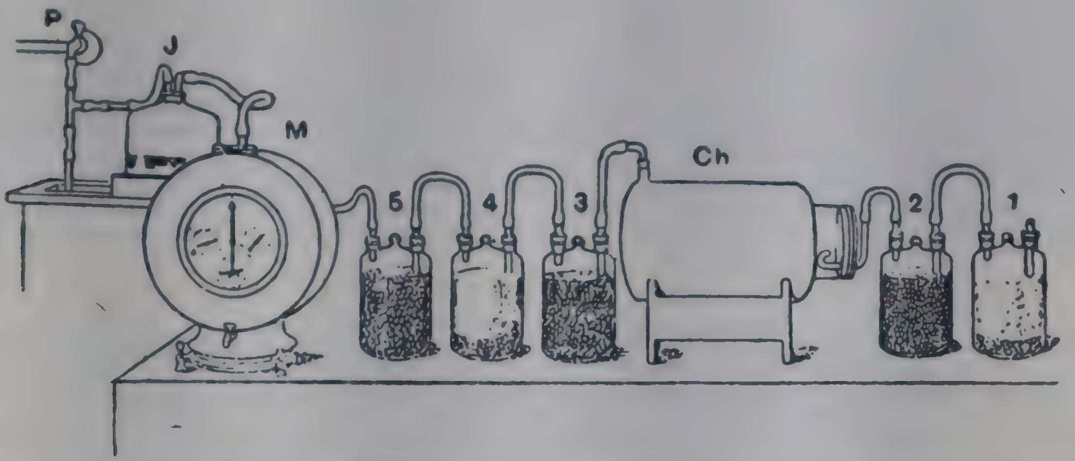

Fig. 12.14—The original Haldane chamber open-circuit gravimetric method.

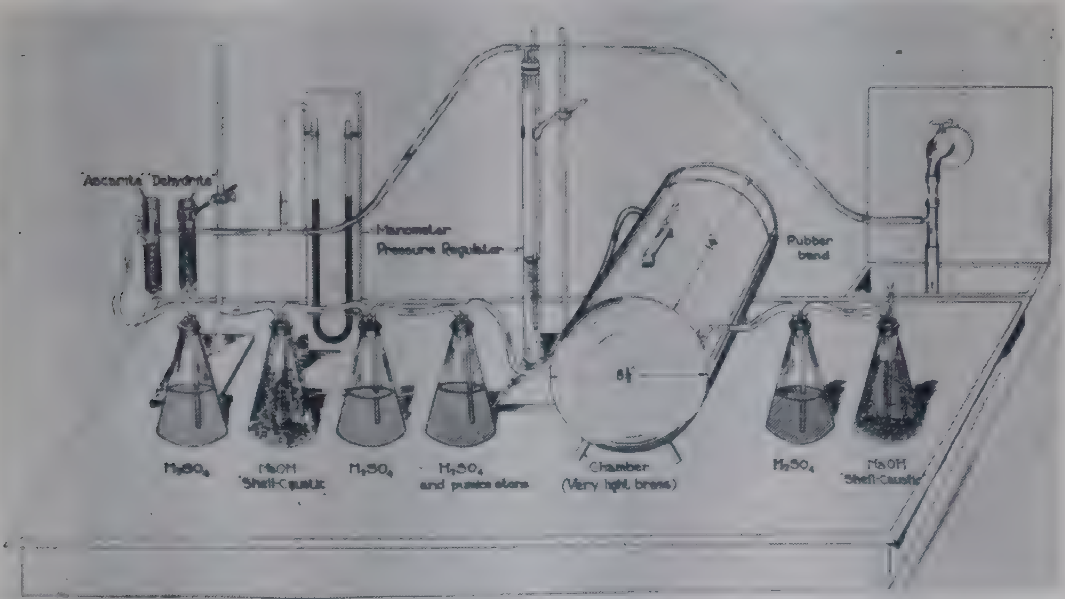

Fig. 12.15—A modification of Haldane apparatus employed for measuring the metabolism of rabbits and chickens.

The numerical computation is a bit involved; it is therefore discussed in detail.

Numerically, the O_2 consumption is the difference between the H_2O and CO_2 gain in absorbers 3, 4, and 5 on one hand and loss in weight of the animal and chamber on the other. Thus

H_2O and CO_2 gain by absorbers 3, 4, and 5	5.32 g
Weight loss by animal and chamber	2.91 "
The O_2 consumed is, therefore	2.41 "

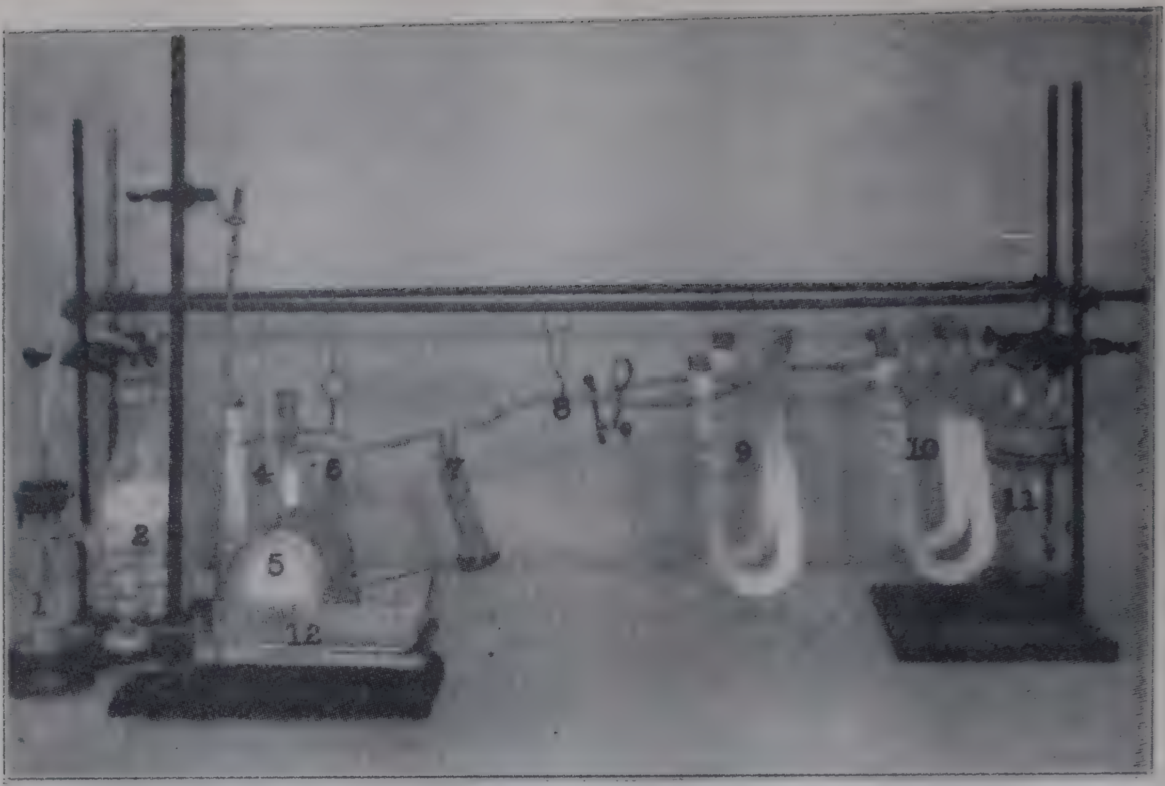

Fig. 12.16—A Haldane metabolism apparatus we used for rats. Number 5 is the chamber (a No. 5 Kerr Mason jar resting on a light tin platform). The train preceding #5 frees the incoming air from H_2O, CO_2; the train following #5 absorbs the H_2O, CO_2 liberated by the rat. The increase in weight of trains 5 to 10 inclusive represents O_2 consumed; 6 to 7, H_2O vaporized; 9 to 10, CO_2 exhaled.

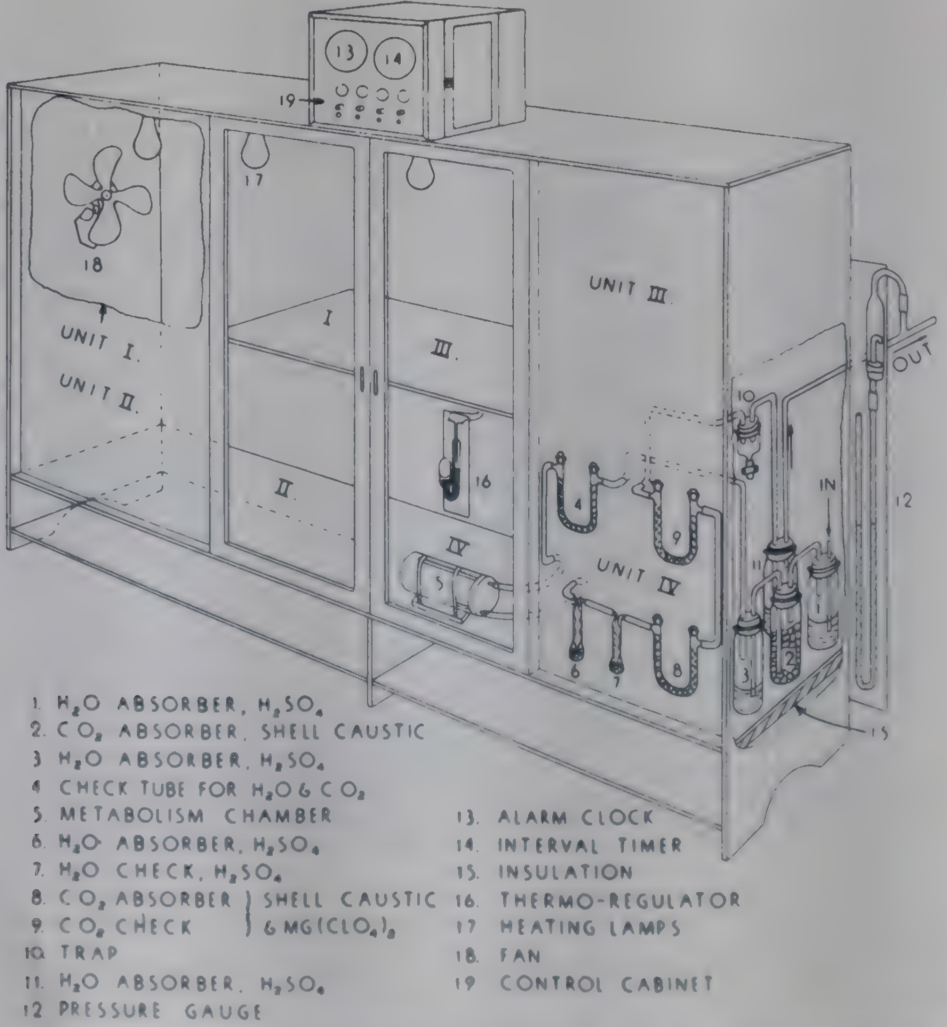

Fig. 12.17a—The four-chamber Haldane apparatus now employed by us for measuring the metabolism of rats in a constant-temperature cabinet. To avoid confusion, only one chamber is shown in the cabinet. For photographs see Figs. 12.17b and c.

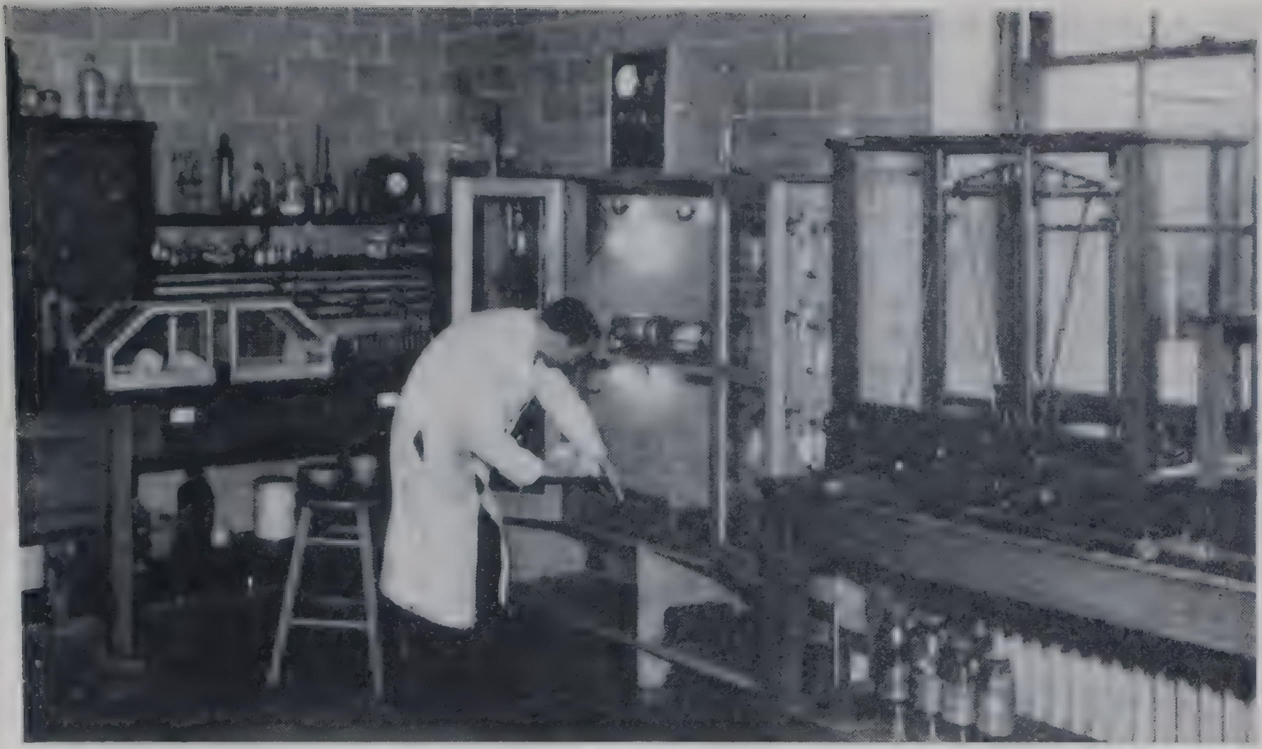

Fig. 12.17b—Represents our 4-chamber Haldane gravimetric apparatus in a constant-chamber cabinet. See Figs. 12.17a and c.

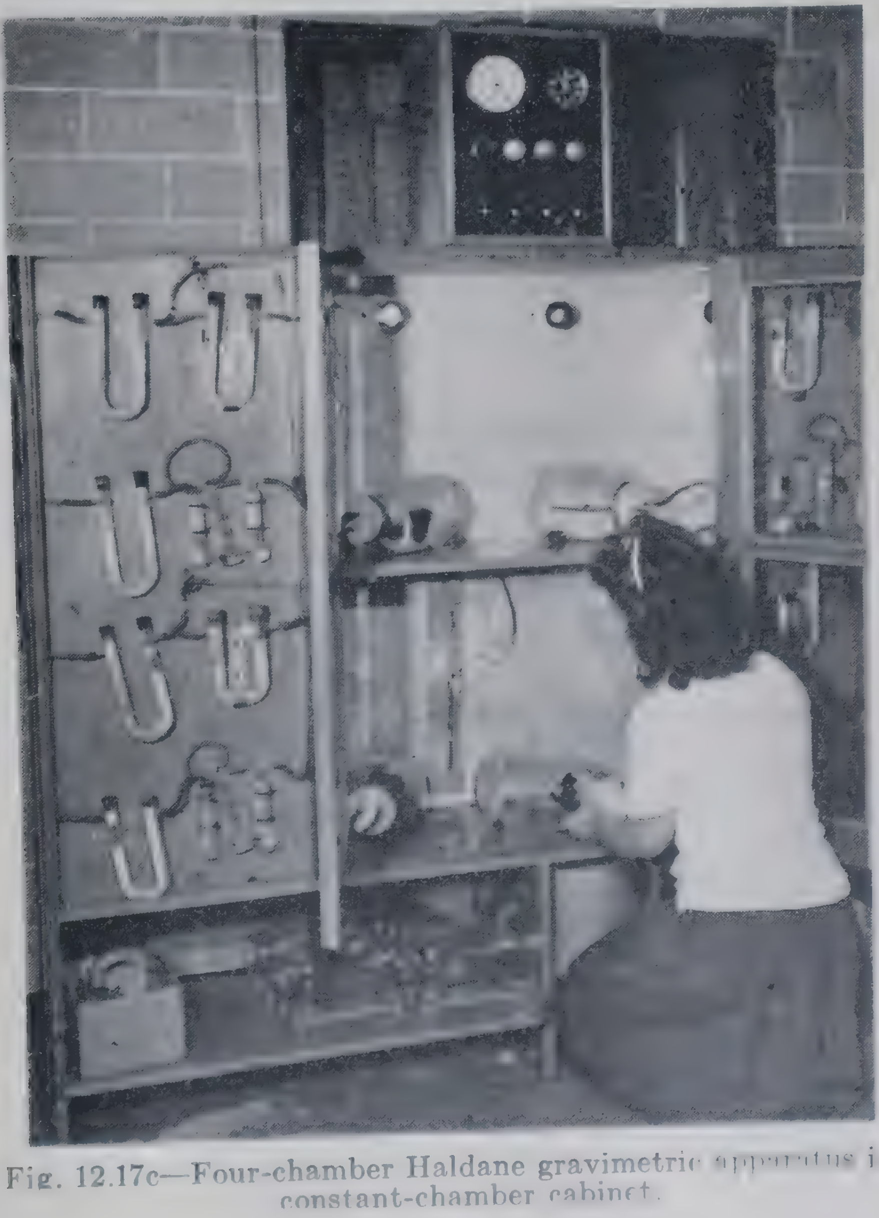

Fig. 12.17c—Four-chamber Haldane gravimetric apparatus in a constant-chamber cabinet.

The H_2O lost by the animal, bottle 3, is easily weighed on an analytic balance; so is the CO_2 lost, by weighing bottles 4 and 5. But the weighing of the animal (together with the chamber) at the beginning and end of the respiration trial with the requisite precision is not easy. Hence, when CO_2 alone suffices (when the R.Q. is known or when comparative results alone are desired), this method is extremely satisfactory; but when it is also necessary to get the R.Q., that is, when it is necessary to determine the O_2 consumed, a large damped analytic balance (Fig. 12.17b) and considerable care in weighing are required.

The following computation example, modified from Haldane, outlines the work in detail. The data are for a 2.5-kg cat for a one-hour trial, with an air-ventilation rate of 720 liters per minute.

Weight of animal and chamber at beginning	6903.86 g
" " " " " "end	6900.95 "
Weight loss by animal and chamber	2.91 "
Weight of H_2O absorber (flask #3) at beginning	3733.47 g
" " " " " " "end	3735.93 "
H_2O lost by animal	2.46 "
Weight of CO_2 absorbers (flasks 4 and 5) at beginning	5839.92 g
" " " " " " " " "end	5842.78 "
CO_2 produced by animal	2.86 "
Sum of H_2O and CO_2	5.32 g
Loss in weight of animal and chamber	2.91 "
O_2 consumed	2.41 "

$$\text{R.Q.} = \frac{\text{g } CO_2 \text{ produced}}{\text{g } O_2 \text{ consumed}} \times 0.727 = \frac{2.86}{2.41} \times 0.727 = 0.86$$

$$\text{Note that the:} \quad \text{R.Q.} = \frac{\text{g } CO_2}{\text{g } O_2} \times \frac{\text{mol. wt. } O_2}{\text{mol. wt. } CO_2} = \frac{\text{gm } CO_2}{\text{gm } O_2} \times 0.727$$

Knowing the R.Q., the caloric equivalent of the CO_2 may be found in Table 12.1.

The following example[25] indicates the type of errors involved in measuring the metabolism of rats by this method. The relative precision for the O_2 determination is greater for small animals (rats) than for large (fowl).

During a 240-minute period a 238-gram rat produced 1.208 g., CO_2 and 1.220 g O_2; $\text{R.Q.} = \frac{1.208}{1.220} \times 0.727 = 0.720$. From Table 12.1, at this R.Q., 1 g CO_2 = 3.33 Cal. The heat production is then $1.208 \times 3.33 = 4.023$ Cal in 240 minutes, or $4.023 \times \frac{1440}{240} = 24.14$ Cal per day, or $24.14 \times \frac{1000}{238} = 101.4$ Cal per kg per day.

The chamber and rat weighed about 1000 grams. The weighing was done on a 5-kg balance of 0.5-mg sensitivity. The CO_2 absorbers were weighed on a 200-gram balance to 1 mg. The error in determining CO_2 is then $2/1208 \times 100 = 0.17$ per cent. Allowing a 3-mg error in weighing the chamber and water absorbers, the error for O_2 determination would be $\frac{2+3}{1220} \times 100 = 0.41$ per cent. The error in the R.Q. is then $0.17 + 0.41 = 0.58$ per cent.

The air ventilation was about one liter per minute; the CO_2 was absorbed by "shell caustic"; the moisture was absorbed first by H_2SO_4 and checked by magnesium perchlorate (Fig. 12.16).

12.2.4: Open-circuit chamber method for larger animals involving gas analysis. This method, devised by Pettenkofer[26] (1862), is similar to the Haldane in general design, but as the chamber is too large for weighing and the CO_2 production is too much for absorption, air-flow metering, aliquoting, and gas analysis are employed.

The air coming into the chamber is assumed to contain[27] 0.031 per cent CO_2 and 20.939 per cent O_2; the outgoing air is analyzed for its CO_2 and O_2 content. The rate of air circulation is measured. The percentages of O_2 decrement and CO_2 increment in the outgoing air are computed; the products of these and the ventilation rate is the rate of O_2 consumption and CO_2 production.

This chamber method is illustrated in Figs. 12.25 (Benedict and Ritzman[28]), 12.24 (Grafe[29]), 12.26 (Benedict-Ritzman type used by us for a while). It is also used by Möllgaard, Lefèvre[30], Kleiber[31], Mitchell[32], and in the Pennsylvania respiration-calorimeter[33].

The measurement of the ventilation rate may be done with large commercial gas meters. The aliquoting is a complex matter (see Figs. 12.24 after Grafe, 12.25 and 12.26 after Benedict and Ritzman; and especially the papers cited).

The most time-consuming aspect of the operation is the gas analysis of chamber air, which is outdoor air slightly (about 1 per cent) contaminated with expired air; and a slight error in the analysis of this dilute air is greatly magnified in the computed heat production. The difficulty is increased if the expired air contains combustible gases, as it does in ruminant-exhaled air. We used the Benedict-Ritzman chamber (Figs. 12.25 and 12.26) for a year or two, but discarded it because of the expense for gas analysis, computing, etc., and adopted in its place the closed-circuit volumetric mask method, previously described (Sect. 12.2.1), and also the open-circuit mask method described below.

12.2.5: Open-circuit mask method for larger animals involving gas analysis. This method has been long used for measuring human metabolism;[34] it in-

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[26] Pettenkofer, M., and Voit, C., *Ann. Chem. und Pharm.* 1862. Voit, C., *Z. Biol.* **11**, 532 (1875).

[27] Carpenter, T. M., *J. Am. Chem. Soc.*, **59**, 358 (1937).

[28] Ritzman, E. G., and Benedict, F. G., "Simplified technique and apparatus for measuring energy requirements of cattle," N. H. Agr. Exp. Sta. Bull. 240, 1929. Also, Benedict, Collins, W. E., Hendry, M. F., and Johnson, "A respiration chamber for large domestic animals," *Id.* Tech. Bull. 16, 1920.

[29] Grafe, E., "Ein Respirationsapparat," *Z. Physiol. Chem.*, **65**, 1 (1910).

[30] Lefèvre, J., et Auguet, A., "Le laboratoire de bioenergetique de la Société scientifique d'hygiene alimentaire". *Ann. Physiol. et physico-chim. biol.*, **5**, 318 (1929); **6**, 182 (1930); also *Bull. Soc. Sci. d'hygiene alim.*, **17**, 445 (1929).

[31] Kleiber, M., "The California apparatus for respiration trials with large animals," *Hilgardia*, **9**, 1 (1935).

[32] Mitchell, H. H., and Hamilton, T. S., *J. Agr. Res.*, **45**, 163 (1932).

[33] Armsby, H. P., "The respiration calorimeter at the Pennsylvania State College," *Exp. Sta. Record*, **15**, 1037 (1904); Report Penn. Exp. Sta. 1903–4; Penn. Agr. Exp. Sta. Bull., 104, 1910. Braman, W. W., "The respiration calorimeter," Penn. Agr. Exp. Sta. Bull., 302, 1933.

[34] Du Bois, E. F., "Basal metabolism in health and disease."

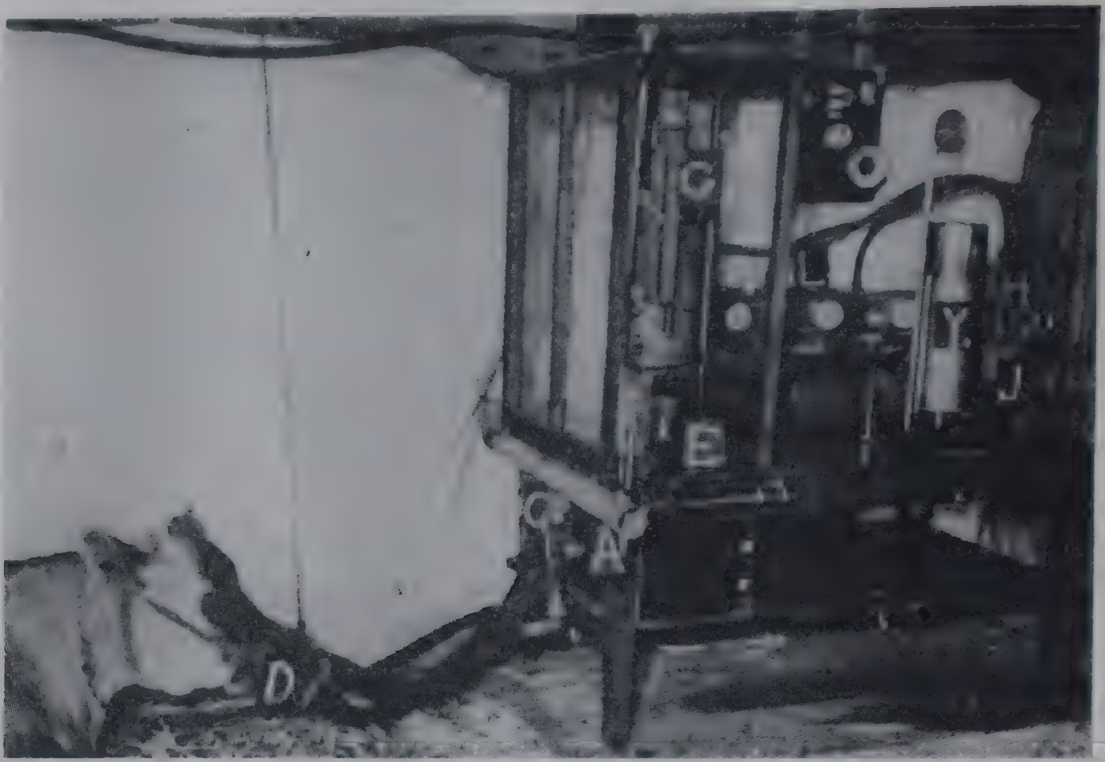
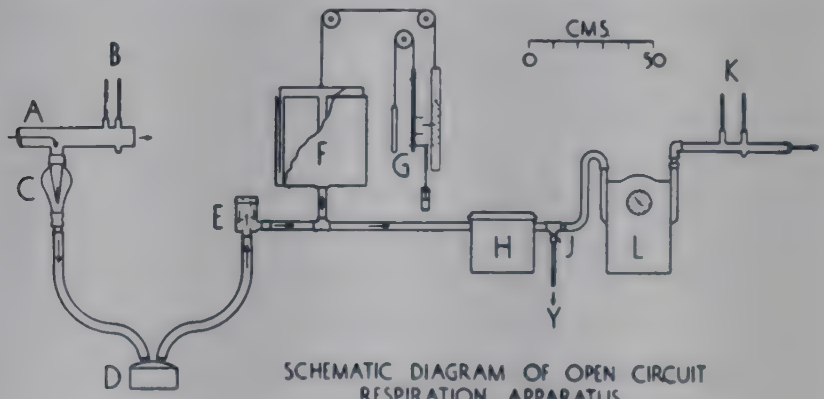
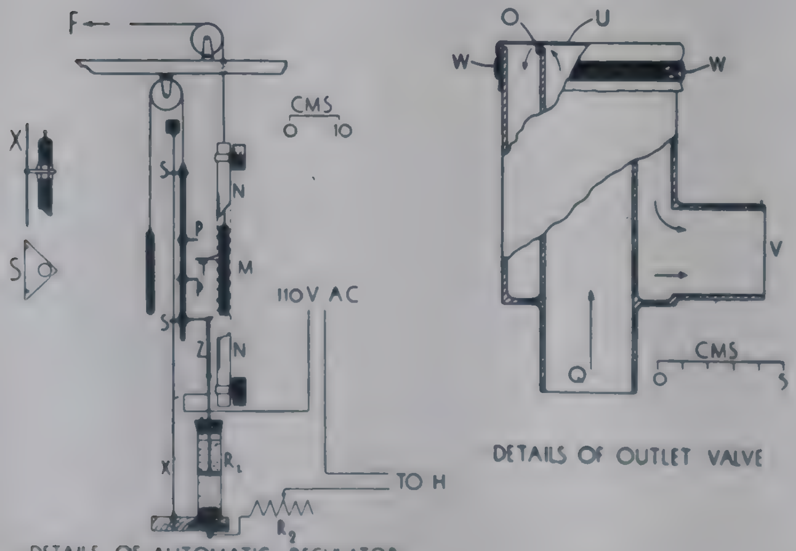


Fig. 12.18a—The open-circuit method for measuring metabolism by passing the expired air through gas meters and analyzing aliquots.



SCHEMATIC DIAGRAM OF OPEN CIRCUIT RESPIRATION APPARATUS



DETAILS OF AUTOMATIC REGULATOR FOR VENTILATING FAN

DETAILS OF OUTLET VALVE

Fig. 12.18b—The open-circuit method for measuring metabolism by passing the expired air through gas meters and analyzing aliquots.

volves collection of all the expired air into a Douglas[35] bag (Fig. 12.19a) or into a Tissot spirometer[36] (Fig. 12.19b) over a short period. The analysis of directly expired air, containing several per cent CO_2 increment and O_2 decrement, is very much simpler than that of chamber air containing a fraction of a per cent of CO_2. The analysis of the chamber air has to be at least ten times as precise (to 0.002 per cent) as of directly expired air (0.02 to 0.05 per cent). We[37] therefore adopted for open-circuit measurements the mask method involving the analysis of directly expired air.

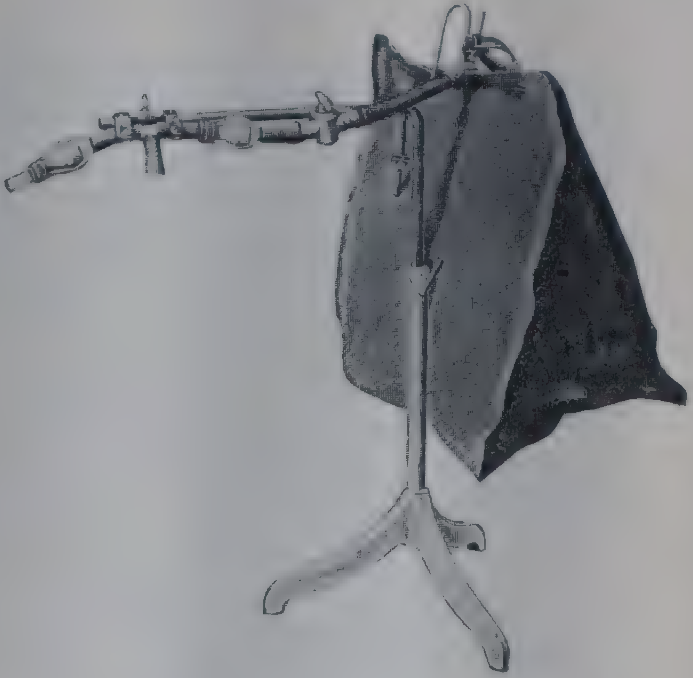


Fig. 12.19a—Open-circuit method for measuring metabolism by collecting expired air in Douglas bags and analyzing the gas by a gas analyzer.

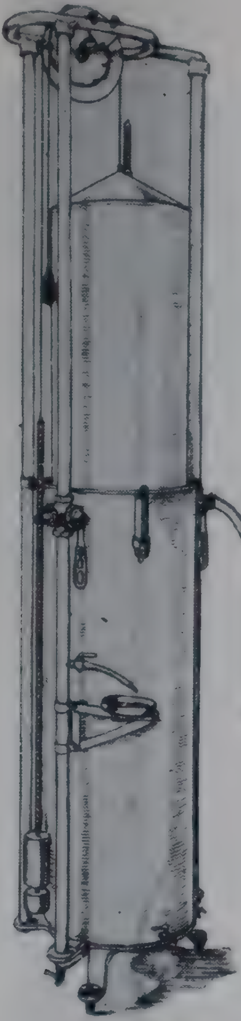


Fig. 12.19b—Open-circuit method for measuring metabolism by collecting expired air in Tissot spirometer and analyzing the gas.

The method we used differs from those used for measuring human metabolism in that the Tissot spirometer and Douglas bag are too small for collecting all the expired air from large farm animals, such as cattle; it was therefore necessary to employ an aliquoting apparatus, as illustrated[38] in Figs. 12.18a and b.

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[35] Douglas, C. G., "A method for determining the respiratory exchange in man," *J. Physiol.*, **42**, 17 (1911).

[36] Tissot, J., "Nouvelle méthode de mésure et d'inscription du débit et des mouvements respiratoires de l'homme et des animaux," *J. phys. et path. gen.*, **6**, 688 (1904); "Appareil pour mésurer le débit et les échanges respiratoires," *Arch. de physiol.* (1896).

[37] Washburn, L. E., and Brody, S., and Ragsdale, A. C., Univ. Missouri Agr. Exp. Sta. Res. Bulls. 263, 1937, and 295, 1939.

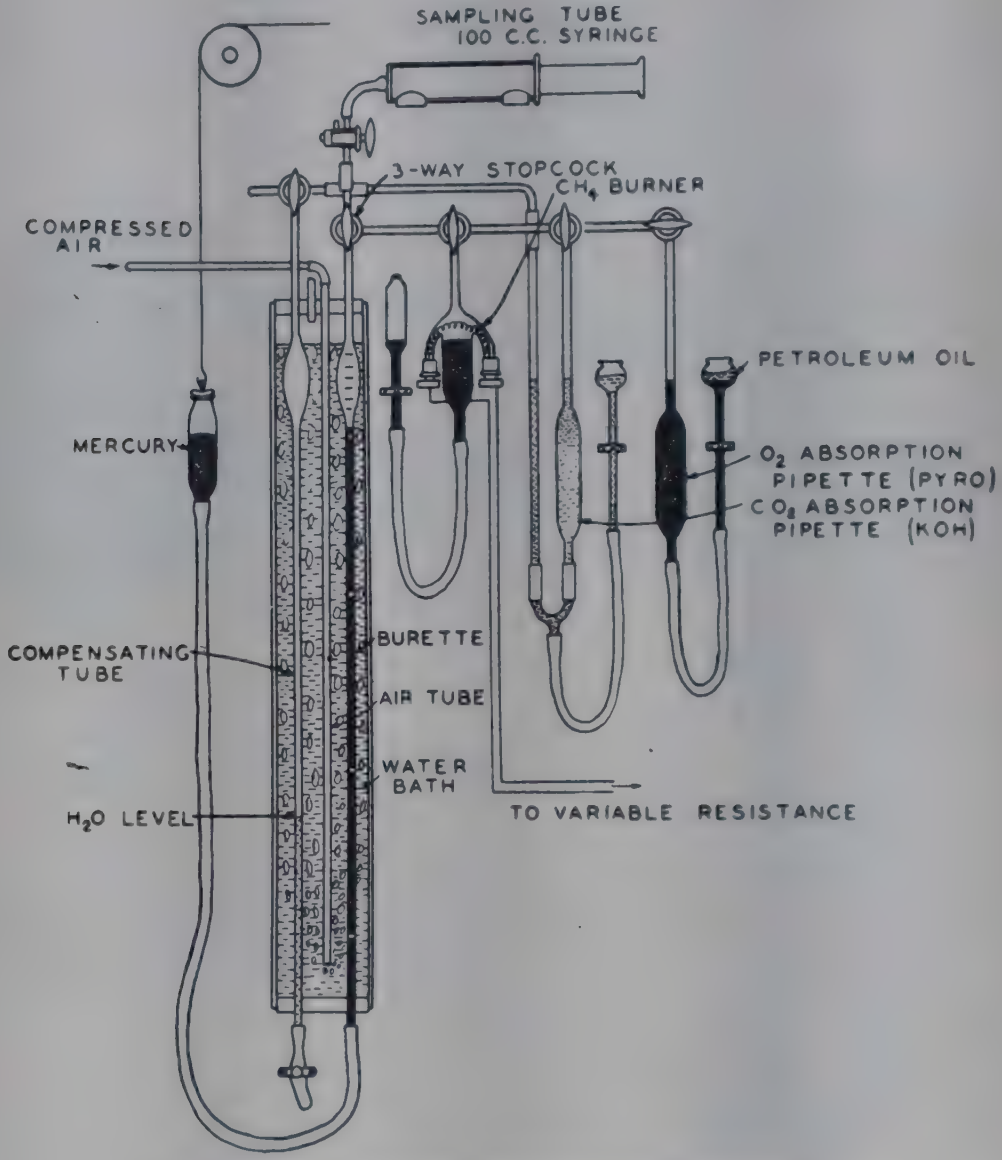

Fig. 12.20a—Haldane gas-analysis apparatus.

12.2.6: Chemical method of analysis of expired air with some illustrative results on cattle. There is a large literature[39] describing chemical methods of gas-analysis. Practically all methods are but slight modifications of the original, 1897 Haldane apparatus, and we employed the Haldane apparatus.

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[38] See, Mo. Res. Bull. 263.

[39] See Haldane, J. S., "Some improved methods of gas analysis," *J. Physiol.*, **22**, **33** (1897–8); "Methods of air analysis," London, 1912. Henderson, Y., *J. Biol. Chem.*, **33**, 31 (1918); Bailey, C. V., *J. Lab. and Clin. Med.*, **6**, 657 (1921). Boothby, W. M., and Sandiford, "A laboratory manual on the technic of basal metabolism rate determinations," Philadelphia, 1920. Brunck, O., Winkler's "Lehrbuch der technischen Gasanalyse," Leipzig, 1927. Carpenter, T. M., *J. Biol. Chem.*, **83**, 211 (1929). Klein, W., and Steuber, Maria, "Die gas analytische methodik des dynamischen stoffwechsels," Leipzig, 1925. Kleiber, M., *J. Biol. Chem.*, **101**, 583 (1933). Winchester, C. F., *Rev. Sci. Instruments*, **9**, 134 (1938). Kraus, E., "Lehrbuch der Stoffwechsel methodik," Leipzig, 1928.

The following paragraphs describe the apparatus especially for analysis of exhaled air from cattle involving analysis for CH_4.

The Haldane gas-analysis apparatus (Fig. 12.20) is composed of a 10-cc burette in which the gas sample is confined. This burette is connected to a leveling bulb wherewith the gas sample can be drawn in or forced out, and to two 30-cc absorbers, one for CO_2 and one for O_2. The burette is also connected to a combustion pipette for oxidizing the CH_4 to CO_2. The CO_2 absorber contains a 20 per cent solution of KOH; the O_2 absorber contains a solution made by dissolving 10 g pyrogallic acid[40] in 100 cc saturated solution of KOH (Sp. gr. 1.55). Temperature, barometric pressure, and water-vapor changes are adjusted by a compensating tube of the same size and shape as the gas burette. Both burettes are kept in a water bath. Some distilled water is kept in the compensating burette. The potash-absorption pipette connects the air between the control and sample tubes. The CH_4 is burned by heating the platinum wire in the combustion pipette to white heat (from a 4-volt current). The resulting CO_2 is measured by absorption in the KOH burette, and CH_4 computed from the equation:

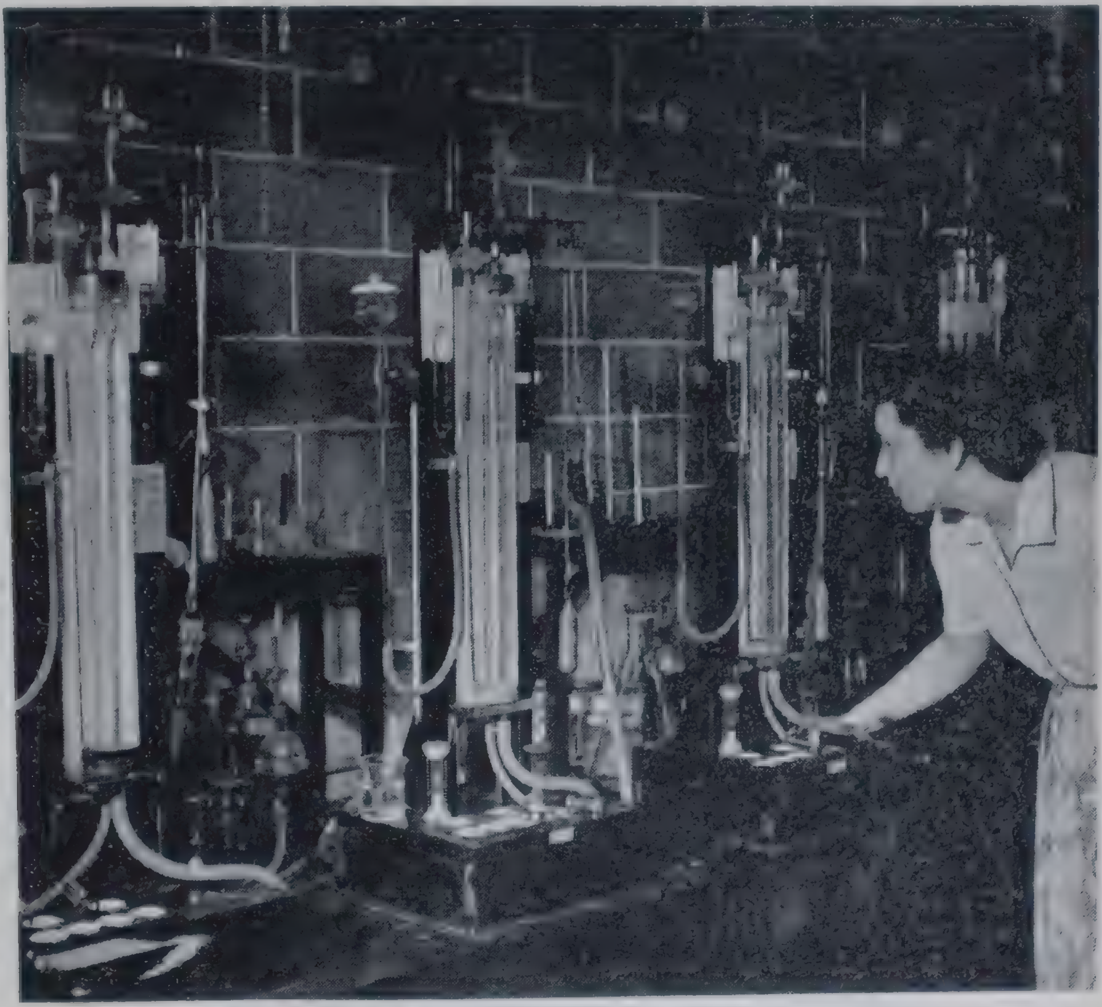

Fig. 12.20b—Haldane gas-analysis apparatus.

$$CH_4 + 2O_2 = CO_2 + 2H_2O \qquad (12.1)$$

From the above equation, 1 volume (or 1 mol) CH_4 produces 1 volume CO_2, so that the

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[40] Other O_2 absorbents may be used, as stick phosphorus, or alkaline $Na_2S_2O_4$ solution.

CH_4 per cent is the percentage ratio of the volume CO_2 formed in combustion divided by the total gas sample; or in equation form,

$$\% \, CH_4 = \frac{\text{vol. } CO_2 \text{ formed in combustion}}{\text{total volume of gas sample}} \times 100 \tag{12.2}$$

$$= \frac{\text{vol. shrinkage due to combustion}}{2(\text{total volume of gas sample})} \tag{12.3}$$

$$= \frac{\begin{array}{c}\text{vol. shrinkage due}\\ \text{to combustion}\end{array} + \begin{array}{c}\text{vol. } CO_2 \text{ formed}\\ \text{in combustion}\end{array}}{3(\text{total volume of gas sample})} \tag{12.4}$$

Equation (12.2) follows from the fact, shown in equation (12.1), that, discounting the H_2O which condenses, 1 volume CH_4 produces 1 volume CO_2; equation (12.3) follows from the fact, shown by equation (12.1), that the volume of CH_4 present is $\frac{1}{2}$ the contraction on combustion; equation (12.4) follows from the fact, shown by equation (12.1), that when the CO_2 has been absorbed, there is a diminution of $\frac{1}{3}$ of the volume.

Equation (12.1) also shows that twice as much O_2 as CH_4 disappears in the combustion of CH_4.

In the following computation, it is assumed that the inspired air is pure outdoor air which contains 0.031 per cent CO_2, 20.93 per cent O_2 and 79.04 per cent N_2, and that no change occurs in the volume of N.

The following computations illustrate the methods and results.

Analysis of barn-yard air (1–16–38)

Volume of air taken into burette	9.663 cc
Volume after CO_2 absorbed	9.659 cc
CO_2 absorbed*	.004 cc
% CO_2	.04*
Volume after O_2 absorbed	7.633 cc
O_2 absorbed	2.026 cc
% O_2	20.97*
% N_2 = 100 − (.04 + 21.04) =	78.92*

* It is usually assumed that *pure* outdoor air contains 0.031 per cent CO_2, 20.94 per cent O_2 and 79.03 per cent N. It is very important to have appreciable amounts of acidulated water in the burette, or the burette becomes alkaline and stores CO_2, with resulting apparently low CO_2 values.

Analysis of directly expired air (by mask, valves, gas meters) for CO_2, CH_4, O_2 and computation of R.Q., and heat production.

Guernsey Cow 428, February 7, 1938, Weight 765 lbs

I. Cow 428 on normal feed intake

Volume air passed through gas meters in 30 min	2378.75	lit
Average meter temperature	29.5° C	
Barometric pressure	753.6	mm
Correction factor[41] for converting to Standard Temperature and Pressure	0.858	
Expired air at STP = 2378·75 × 0·858 (lit/30 min)	2043.4	lit
Expired air as at STP (lit/min)	68.1	
Volume expired air sample in the Haldane 10-cc analyzer	10.004	cc
Volume after CO_2 absorbed	9.727	cc
CO_2 absorbed	0.277	cc
% CO_2 in exhaled air	2.77	

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[41] See Table 8, p. 55, Carpenter's "Tables, factors and formulas for computing respiratory exchange and biological transformations of energy." *Carnegie Inst. Washington Publ.* 303A.

Volume after combustion of CH_4 and absorption of resulting CO_2	9.648 cc
CH_4 produced = $\frac{1}{3}$ (9.727 − 9.648) [see eq. (12.4)]	0.026 cc
% CH_4 in expired air	0.26
Volume after O_2 absorbed	7.858 cc
O_2 absorbed = 9·648 − 7·858 =	1.790 cc
Total O_2 absorbed, including that used for oxidation of CH_4 = 1.79 + 2 × 0.026 =	1.842 cc
[see eq. (12.1) indicating twice as much O_2 absorption as CH_4 oxidation]	
O_2 in expired air	18.41 %
N_2 in expired air = 100 − (2.77 + 0.26 + 18.41) =	78.56 %

To compute the volume of O_2 retained by the animal, the volume of O_2 expired is deducted from the volume of O_2 inspired.

The total volume of expired air for the 30-minute period, as measured by gas meters and corrected to standard conditions of temperature and pressure, is 2043.4 liters.

The percentage of N_2 in this sample of expired air is 78.56 per cent, as compared to 79.03 per cent, the known percentage in outdoor air. Since N_2 is not retained by the animal, the same volume (STP) of N_2 is expired as is inspired. The decrease in the percentage of N_2 expired over that inspired means that the total volume of air expired was different (more in this case) from the total volume inspired. The reason for the change in volume in the air, on passage through the lungs, is that the R.Q. is *not* equal to 1.

The air inspired during the 30-minute period must have had such volume that the N_2 percentage was 79 03 per cent instead of 78.56 per cent, the percentage found in expired air. The volume of inspired air may (having 79.03 per cent N_2) be computed by the inverse proportion:

$$\text{Vol. inspired air} : \text{Vol. expired air} :: 78.56 : 79.03$$

$$\text{Therefore volume of inspired air} = \frac{78.56}{79.03} \times 2043.4 = 2031.2 \text{ liters}^{42}.$$

The content of outdoor air is 20.94 per cent. Therefore

$$\begin{array}{lr} \text{Volume } O_2 \text{ in outside air inspired (STP)} = 2031.2 \times .2094 = & 425.33 \text{ lit} \\ \text{Volume } O_2 \text{ in expired air (STP)} = 2043.4 \times .1841 = & \underline{375.19} \text{ ``} \\ \text{Volume } O_2 \text{ consumed by animal} = & 49.14 \text{ ``} \end{array}$$

The O_2 consumed expressed as a percentage of expired air is then:

$$\frac{49.14}{2043.4} \times 100 = 2.40\%$$

The excess of CO_2 expired over CO_2 inspired can be computed in the same manner. The CO_2 in outdoor air is approximately 0.03 per cent.

$$\begin{array}{r} \text{Volume } CO_2 \text{ in expired air} = 2043.4 \times .0277 = 56.60 \text{ lit} \\ \text{Volume } CO_2 \text{ in inspired air} = 2031.2 \times .0003 = 0.60 \text{ ``} \\ CO_2 \text{ increment} = 56.00 \text{ ``} \end{array}$$

$$CO_2 \text{ increment as a percentage of expired air} = \frac{56}{2043.4} \times 100 = 2.74\%$$

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[42] Table 11, "Volumes of oxygen in incoming air corresponding to 100 volumes of outgoing air with different percentages of nitrogen. 79.03:%N_2 = 20.94:X", in Carpenter's Tables[41] will be helpful in these computations.

The correction due to volume change is so small that it may be neglected and the percentage CO_2 increment may be obtained by subtraction prior to correction thus:

$$\% CO_2 \text{ increment} = 2.77\% \text{ in expired air } 0.03\% \text{ in inspired air} = 2.74\%$$

$$\text{R.Q.} = \frac{CO_2 \text{ increment}}{O_2 \text{ retained}} = \frac{2.74}{2.40} = 1.14$$

The heat production is the volume of expired air × % O_2 decrement times thermal equivalent of the O_2 at the given R.Q. = 2043.4 × .024 × 5.047 = 247.5 Cal in 30 minutes, or 11,880 Cal/day.

We next proceed to illustrate another analysis on the same cow 428 after she had fasted for two days, with a consequent decrease in R.Q. from over 1 to near 0.8, so the N_2 per cent is increased on passing through the pulmonary system, because less CO_2 is produced than O_2 is consumed.

II. Cow 428 after 2 days' fast

Volume of air passed through gas meter in 30 minutes	1330.5 lit
Average meter temperature	32.8° C
Barometric pressure	743.6 mm
STP correction factor	0.830
Expired air as at STP, 1330.5 × 0.830	1104.3 lit/30 min
Vol. expired air sample in gas burette	9.670 cc
Vol. after CO_2 absorbed	9.490 cc
CO_2 absorbed	0.180 cc
% CO_2 in exhaled air	1.86
Volume after combustion of CH_4 and absorption of resulting CO_2	9.481 cc
CH_4 produced = $\frac{1}{3}$ (9.490 − 9.481)	0.003 cc
% CH_4 in expired air	0.03
Volume after O_2 absorbed	7.679 cc
O_2 absorbed (9.481 − 7.679)	1.802 cc
Total O_2 absorbed in alkali, including that used for CH_4 oxidation, 1.802 + 2 × 0.003 =	1.808 cc
O_2 in expired air	18.70 %
N_2 in expired air = 100 − (1.86 + 18.70 + 0.03) =	79.41 %
O_2 consumed 20.94 − 18.70 =	2.24 %

$$\text{Apparent R.Q.} = \frac{1.86 - .03}{2.24} = \frac{1.83}{2.24} = 0.821$$

The R.Q. corrected for volume changes may be computed by an analogous but shorter method than that previously explained, as follows:

R.Q. corrected for changes in N_2%: corrected O_2 in inspired air =

$$20.94 \times \frac{79.41}{79.03} = 21.04$$

"True" R.Q., that is, R.Q. corrected for volume changes =

$$\frac{1.86 - 0.03}{21.04 - 18.70} = \frac{1.83}{2.34} = 0.78$$

$$\begin{aligned}\text{Heat production} &= 1104.3 \times 0.0234 \times 4.776\\ &= 123.4 \text{ Cal in 30 minutes}\\ &= 5923 \text{ Cal/day}\end{aligned}$$

12.2.7: Electric methods of gas analysis. The Haldane method of gas analysis, and especially its modification for analysis of chamber air such as

Carpenter's, is exacting and time-consuming. The electrometric method here discussed is simple and rapid in operation, but difficult in adaptation and calibration.

The history, principles, and application of the method may be obtained from Palmer and Weaver's monograph[43]. This method is based on (1) differences in thermal conductivity of different gases, and (2) differences in electrical resistance of wires at different temperatures, with the result that (3) if the wire has a high temperature coefficient of electrical resistance, this resistance will have a value corresponding to the thermal conductivity; therefore this resistance will have a value corresponding to the composition of the gas surrounding the wire.

This method then consists in comparing the resistance of two electrically heated wires, surrounded respectively by the gas under investigation, and by a standard or reference gas. The resistance of the two wires is compared by galvanometer, voltmeter, or potentiometer. The readings are calibrated empirically in terms of percentage composition of the gas under investigation under the given conditions.

The greater the difference in conductivity between the components of the gas under investigation the greater the precision of the measurement. The following arbitrary values (ratio of the product of potential difference and current of given gas to that of air when the resistance is 5.66 ohms, wire temperature 100° C, and temperature of chamber wall surrounding the wires 30° C) indicate the relative power losses in various gases: air, 1.000; CO_2, 0.697; N_2, 0.991; O_2, 1.024; SO_2, 0.440; H_2, 6.613. Because N_2 and O_2 and air have nearly the same thermal conductivity, this method is not sensitive for evaluating the O_2 per cent in air. But it is suitable for evaluation of CO_2 because the thermal conductivity of CO_2 differs considerably from that of air. These differences are illustrated in Fig. 12.21. This method is rapid, the results may be recorded automatically in the absence of an operator, and the readings are independent of atmospheric pressure. It has been used successfully for CO_2 determination in alveolar air ("alveolar air indicator" or "Katharometer")[44] and also in normally expired air[45].

The "Katharometer"[46] measures the resistance in an unbalanced wheatstone bridge by the deflection of the needle of a millivoltmeter. In other commercial instruments[47], the resistance in a wheatstone bridge is balanced by using a slide wire to bring a galvonometer to zero deflection.

Carpenter[48] described a modification of Noyons' "diaferometer thermique"[49] for analysis of both CO_2 and O_2. The measurements are based on the deflections of a sensitive galvanometer which indicates changes in resistance of platinum wires caused by differences in the cooling power of the gases surrounding the wires. It is not recommended for use in the presence of CH_4, H_2, or CO. This apparatus, like the others, has to be checked by the chemical method of gas analysis.

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[43] Palmer, P. E., and Weaver, E. R., "Thermal-conductivity method for the analysis of gases," *U. S. Dept. of Commerce, Technologic papers of the Bureau of Standards*, 249, 1924.

[44] Daynes, H. A., and Hill, A. V., *Proc. Roy. Soc.*, **97B**, 273 (1920); *J. Physiol.*, **56**, p. xx (proceedings) (1922).

[45] Rabinowitch, I. M., and Bazin, E. V., *J. Canadian Med. Assn.*, **16**, 638 (1926).

[46] Manufactured by the Cambridge Instrument Co., Ossining-on-Hudson, N. Y.

[47] Rosecrans, C. Z., "Automatic gas analysis recorder for the range of 0 to 3.5 per cent of CO_2 in air," *J. Optical Soc. of America & Review of Sci. Instruments*, **14**, 479 (1927) (Leeds & Northrup Co., Philadelphia). Ledig, P. G., and Lyman, R. S., "An adaptation of the thermal conductivity method to the analysis of respiratory gases," *J. Clinic. Inv.*, **4**, 495 (1927).

[48] Carpenter, T. M., and Corpatchinsky, V. S., *Ind. Eng. Chem., Analytical Ed.*, **14**, 159 (1942).

[49] Noyons, A. K. M., *Ann. Physiol. physico-chim. biol.*, **13**, 909 (1937).

12.3: Food calorimetry. The gross energy value of a feed or food may be determined either by (1) *direct calorimetry*, by burning a sample in a water-jacketed chamber and measuring the rise in the water temperature, or (2) *indirect calorimetry*, by burning the sample in a "respiration" apparatus having a combustion chamber instead of a pulmonary system of an animal, and measuring the O_2 consumed, and/or CO_2 produced, and then computing the heat production from the thermal values of the O_2 for the given R.Q. (Table 12.1).

The direct method, devised by Berthelot, is the more commonly used[50]. It is called a bomb calorimeter because the weighed sample is placed in a heavy steel "bomb" charged with O_2 under pressure (at least 20 atmospheres). The energy content of the sample is computed from the temperature rise of the surrounding water, weight of the water, heat capacity of the apparatus, and related corrections.

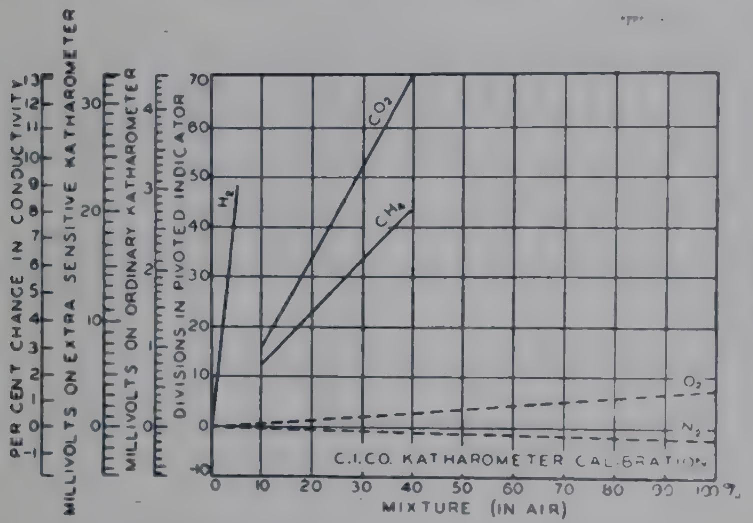

Fig. 12.21—Katharometer calibration chart, for electrometric (thermal conductivity) analysis of expired air.

Benedict[51] devised an indirect method similar in principle to the Benedict clinical metabolism apparatus. It consists (Fig. 12.22) of (1) a combustion chamber, *A*, (corresponding to the pulmonary system in the Benedict-Collins clinical metabolism apparatus) in which the sample is burned; (2) soda lime, *B*, for absorbing the CO_2; (3) air-tight motor blower; and (4) spirometer, *P*. The energy content of the sample is computed from the O_2 used for the combustion, and from the thermal values of O_2 as given by Benedict (determined with the aid of the bomb calorimeter).

12.4: Historic comments. As noted in the introductory quotation, Lavoisier is the founder of biocalorimetry. It was not, however, until about 1850 that this work was taken up again with the appearance of the Regnault and Reiset practical biocalorimetric methods (Fig. 12.10).

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[50] Fries, J. A., "Use of the bomb calorimeter," U. S. Dept. Agr. Bull. 94, 1907, and standard books.

[51] Benedict, F. G., and Fox, E. L., "The oxycalorimeter for fuels, foods, and excretory substances." *Ind. and Eng. Chem.*, **17**, 912 (1925); *J. Biol. Chem.*, **66**, 783 (1925)- Benedict and Farr, A. G., New Hampshire Agr. Exp. Sta. Bull. 242, 1929.

An interesting modification of this closed-circuit apparatus is the *methode de confinement*[52] or the *pneumatische Kammer*[53]. The animal is kept in a closed chamber under constant volume, for example, in a desiccator or under constant pressure, as under a floating bell (Fig. 12.23), and the confined air is analyzed, at the end of a convenient period, for the CO_2 increment and O_2 decrement. According to Lulanie, the CO_2 may be increased to 6 per cent and the O_2 decreased to 11 per cent. Two per cent CO_2 in the atmosphere does not affect metabolism in man[54].

Giaja[55] employed "confinement-method" chambers for animals ranging from mice to men. There are too many types of closed-circuit apparatus for man[56] and laboratory animals[57] to be described here.

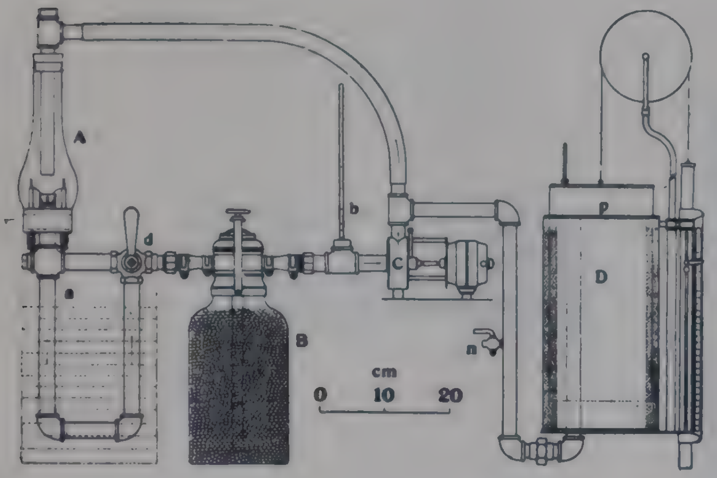

Fig. 12.22—Benedict's oxycalorimeter.

As previously noted, the first modern open-circuit metabolism apparatus was built in 1862 by Pettenkofer and Voit, and the first direct calorimeter, combined with the Pettenkofer open circuit apparatus, in 1894 by Max Rubner.

Following Rubner's completion of the calorimeter for dogs in 1891, Atwater (the first director of the first Federal American experiment station, established in Middletown, Connecticut, in 1875, and the first director, 1888, of the U. S. Office of Experiment Stations) and Rosa (chief physicist of United States Bureau of Standards) began work in this country on a calorimeter for man in 1892, completing it in 1897. With it, Atwater[58] and associates extended Rubner's findings concerning the agreement between observed and computed values for heat production to include man.

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[52] Lulanie, F., *Arch. physiol.*, **6**, 845 (1894). Kaufmann, *Id.*, **8**, 329 (1896). See also *Oeuvres de Lavoisier*, **2**, 326.

[53] Steuber, Marie, "Wissenschaftliches Arch. Landwirtschaft," Abt. B., *Tierernähurng & Tierzucht*, **2**, 34 (1930). Benedict, F. G., and Homans, J., *Am. J. Physiol.*, **28**, 29 (1911). Mattill, H. A., *J. Biol. Chem.*, **55**, 717 (1923).

[54] Benedict and Milner, U. S. Dept. Agr. Bull., 175, 1907.

[55] Giaja, J., *Ann. de physiol. physico-chim. biol.*, **1**, 596 (1925).

[56] *Cf.* Du Bois'[34] and Lusk's[1]. Carpenter, Carnegie Inst., Washington Publ.. 216, 1915.

[57] *Cf.* Benedict, F. G., and Riddle, O., *J. Nut.*, **1**, 497 (1929). Benedict and MacLeod, G., *Id.*, p. 357. Wesson, L. G., *Id.*, **3**, 503 (1931). Greene, J. A., and Luce, R. P., *Id.*, **4**, 371 (1931). Ebeling, A. H., and Corey, R. B., *J. Exp. Med.*, **51**, 41 (1930). Lewis, H. G., and Luck, J. M., *J. Biol. Chem.*, **103**, 209 (1933).

The Atwater-Rosa respiration calorimeter measured the CO_2 production but not the O_2 consumption. The later feature (closed circuit) was developed by Benedict in the Atwater-Benedict respiration calorimeter,[59] thus making it possible to measure the R.Q.

Lusk and associates[60] built two respiration calorimeters, a small one for dogs at the Cornell Medical College and a large one for man at the Bellevue Hospital (now at the New York Medical Center). The later calorimeter, directed by Du Bois from its beginning, is at the time of this writing used for investigating mechanisms of heat loss in the human body.

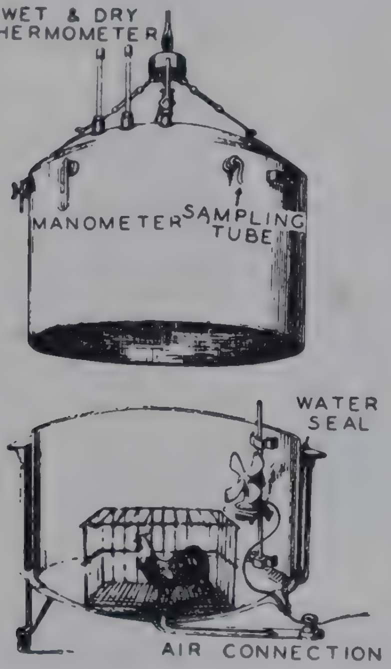

Fig. 12.23—Confinement method for measuring the respiratory exchange (Courtesy Marie Steuber).

It is instructive to note that Rubner (1854–1932), Atwater (1844–1907), and Lusk (1866–1932) were pupils of Carl Voit (1831–1908); that Armsby (1853–1921) was for a time at the Mockern Agricultural Experiment Station under Voit's influence, but directed by Kuhn, Kellner, and Fingerling. Voit was a pupil of Liebig (1803–1873), who had studied under Gay-Lussac (1778–1850), who was in turn a pupil of Berthelot (1748–1822) and Laplace (1749–1827). The latter was a collaborator of Lavoisier (1743–1794).

Armsby[61], the most influential American investigator in farm-animal nutrition, adopted the Atwater-Rosa respiration calorimeter for cattle, with funds provided (1898) by the U. S. Department of Agriculture. The use of this calorimeter began in 1901. It is the only available respiration calorimeter for cattle.

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[58] Atwater, W. O., and Rosa, E. B., "First report of respiration calorimeter," U. S. Dept. Agr. Office of Exp. Stations Bull., xliv, 1897.

[59] Atwater, W. O., and Benedict, F. G., "A respiration calorimeter with appliances for the direct determination of oxygen," Carnegie Inst., Washington Publ. No. 42, 1905.

[60] Williams, H. B., "Animal calorimetry," Paper I. "A small respiration calorimeter," *J. Biol. Chem.*, **12**, 317 (1912); Lusk, G., Riche, J. A., and Soderstrom, G. F., "Clinical Calorimetry." "The respiration calorimeter of the Russell Sage Institute of Pathology in Bellevue Hospital," *Arch. Int. Med.*, **15**, 793, 805 (1915).

[61] Benedict, F. G., "Henry Prentiss Armsby," Biographic memoir. *National Acad. Sc., Biographic memoirs*, Vol. IIX, 1938.

Armsby's calorimeteric contributions revolved about the evaluation of the energy value of feeds for relatively mature cattle. His first work was concerned with testing on ruminants the validity of Rubner's theory (1883) to the effect that carbohydrates, fats, and proteins may replace each other in proportion to their metabolizable energy when fed in submaintenance amounts. These ideas were modified by Rubner's later formulations of the conception of specific dynamic action. Armsby has shown that the specific dynamic action of feeds is greater for ruminants than for man, and that the processes of digestion and assimilation (heat increment of feeding) should be taken into account in the determination of the energy values of feeds. He found (1908) that only 45 per cent of the energy from hay is utilized; the remainder is wasted: 41 per cent in feces, 6.8 per cent in methane, 7.3 per cent in urine. These considerations led Armsby to the concept of net energy values of feeds (Chs. 2 and 5).

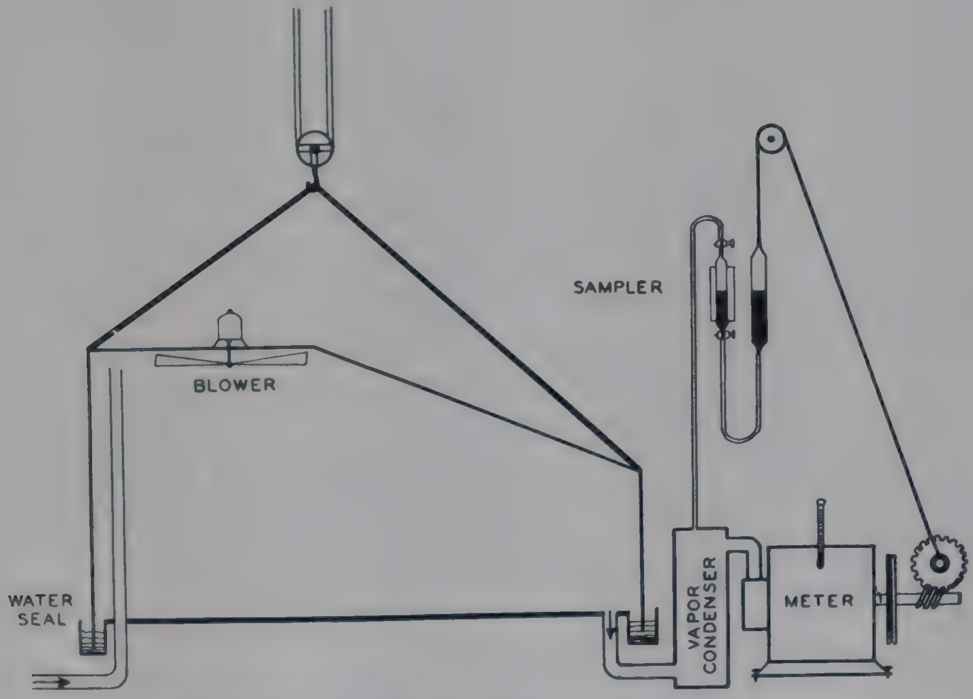


Fig. 12.24—Grafe's open-circuit chamber for measuring the respiratory exchange in large animals.

Other direct calorimeters for farm animals are Deighton's on pigs[62] and on fowl[63] and Barott's[64] on chick embryos and chickens. The respiration calorimeter of Lefèvre and Auguet[30] has been used for man and for sheep.

12.5: Summary and general comments. Biocalorimetric methods are divided into (1) *direct*, involving the measurement of heat dissipation; (2) *indirect*, involving the measurement of heat production from the rates of O_2 consumption and CO_2 production; (3) *mixed*, such as the *partitional calorimetry* (involving the measurement of heat loss by radiation, conduction-convection, and vaporization, and *insensible-perspiration calorimetry* (involving

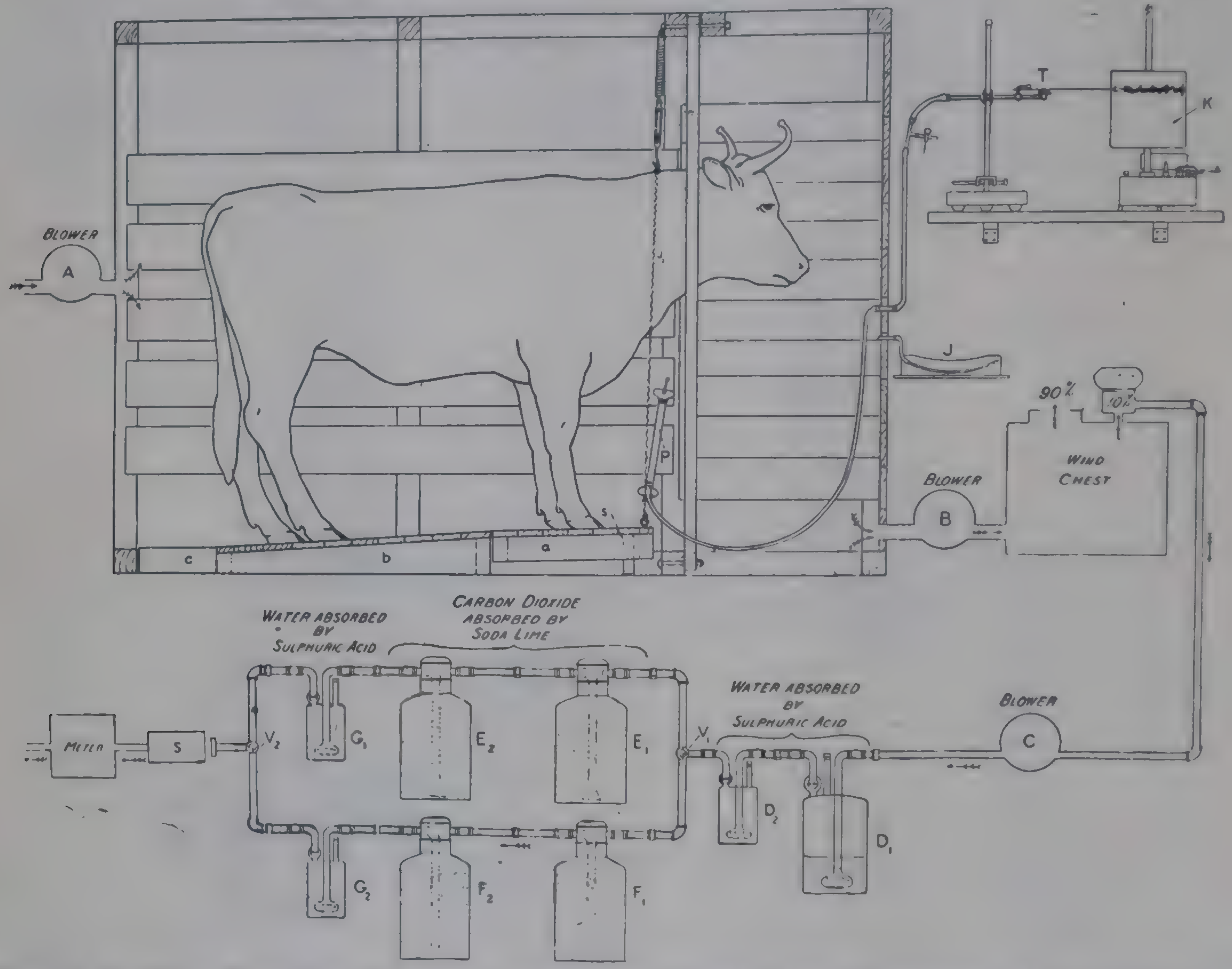
[62] Deighton, T., *J. Agr. Sci.*, **16**, 376 (1926). Hill, A. V., and Hill, A. M., *J. Physiol.*, **48**, p. xiii (1914). Capstick, J. W., *J. Agr. Sci.*, **11**, 408 (1921).

[63] Deighton, T., *J. Agr. Sci.*, **29**, 431 (1939).

[64] Barott, H. G., *et al.*, *J. Nut.*, **11**, 191 (1936); **15**, 145 (1938).

accurate measuring of weight loss of the animal due mostly to water vaporization), both discussed in Chapter 11; (4) *combined*, including both the direct and indirect methods, as in the Pennsylvania respiration calorimeter.

The direct methods may be of the water-cooling or of the compensation type (involving the balancing of heat produced by the animal in one chamber, and by heat produced through measured amounts of electrical energy in the same or another chamber of the same size). The indirect methods may be of the closed-circuit type (involving the rebreathing of air, usually with removal of the CO_2 by circulation through purifers and addition of fresh O_2), or of the open-circuit type (involving the metering and analyzing of the expired air).


BLOWER
A
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WATER ABSORBED BY SULPHURIC ACID
CARBON DIOXIDE ABSORBED BY SODA LIME
METER
S
V_2
G_1
E_2
E_1
V_1
WATER ABSORBED BY SULPHURIC ACID
BLOWER
C
D_2
D_1
G_2
F_2
F_1

Fig. 12.25—The Benedict-Ritzman open-circuit method for measuring the respiratory exchange in large animals.

From the standpoint of scientific interpretability of results, method (4), respiration calorimetry is best. Unfortunately, this method is apparently not practicable for farm animals except for one well-equipped institution in the country; and even in this case the gathering of data is too laborious and slow, to satisfy desires for "practical results" in "reasonable time", and the data are insufficient for statistical analysis.

But even the indirect method (open-circuit respiration-chamber gas analysis) as employed in five laboratories (in U. S., Benedict-Ritzman, Mitchell-Hamilton, Kleiber; in Europe, Möllgaard, Fingerling, Popov-Thome) is too expensive and too slow, and the data obtained are usually not sufficient for statistical analysis. We have therefore adopted for cattle and other farm animals the mask method, similar to those used for measuring basal metabolism in humans, for both closed- and open-circuit work.

The measurement of O_2 consumption alone (closed-circuit spirometer method) is quite sufficient for "normal" animals within the R.Q. limits of 0.71 and 1.0. Within these R.Q. limits the caloric equivalent of O_2 is well known and relatively constant. The caloric value of O_2 may perhaps be constant even above the R.Q. value of 1.0, as pointed out by Benedict[65], who, however, was criticized[66] for this conclusion, and especially for the suggestion that direct calorimetry is unnecessary. There is no doubt that the indirect method is not rigorously sufficient, as when oxygen is used in the body for purposes other than oxidation, such as massive conversion of carbohydrate containing some 53 per cent O_2 to fat containing 11 to 12 per cent, with corresponding apparent depression of O_2 consumption (or raising of the R.Q.). Many agricultural processes consist in such transformation of dietary carbohydrate to body fat[67], milk fat[68], and egg fat.

Then, too, many of the metabolites are not members of the three standard nutrients, carbohydrate, fat, and protein[69]; nor do these substances react according to type, either because of dietary condition[70] or metabolic abnormalities, as in diabetes, with formation of sugar from protein and other sub-

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[65] Benedict, F. G., "Lipogenesis in animals," Carnegie Inst., Washington Pub. 489, 1937. See also Leegaard, F., *Acta Med. Scand.*, **77**, **1** (1931).

[66] Book review, *J. Am. Med. Assn.*, **110**, 1311 (1938).

[67] Lawes, J. B., and Gilbert, J. H., *Trans. Roy. Soc.*, **2**, 493 (1859). Trowbridge, P. F., Moulton, C. R., Hogan, A. G., Haigh, L. D., *et al.*, Univ. Missouri Agr. Exp. Sta. Res. Bulls. 55, 61, 73, and others. Benedict,[65] (1937). (R.Q. 1.47 for fattening geese.) Wierzuchowski, M., and Ling, S. M., *J. Biol. Chem.*, **64**, 697 (1925) (R.Q. 1.58 for fattening hogs). Rapport, D., *et al.*, *J. Biol. Chem.*, **60**, 583 (1924), who quotes M. Bleibtrau [*Pflüger's Arch.*, **85**, (1901)], obtaining R.Q. 1.38, and Bleibtraub's correction equation for conversion of C.H. to fat:

$$270.06 \text{ g glucose} \rightarrow 100 \text{ g fat} + 54.61 \text{ g } H_2O + 115.45 \text{ g } CO_2$$

In this transformation of carbohydrate to fat, it is assumed that 60.7 Cal, or 6 per cent of the energy of carbohydrates is lost. The heat of combustion of fat was assumed to be 9.50 Cal/g, and of glucose 3.743 Cal/g. The suggestion is made to multiply the excess CO_2 liters above the R.Q. of 1 by 0.8 Cal and add the product to the calculated heat value of the protein and C.H. which are being oxidized. A liter of CO_2 above the non-protein R.Q. of 1.0 is supposed to correspond to deposition 1.7 g fat derived from 4.80 g glucose, or from 5.06 g starch. See also Talbot, F. S., *et al.*, *Am. J. Physiol.*, **124**, 246 (1938).

[68] Jordan, W. H., and Jenter, C. G., "The source of milk fat," New York Agr. Exp. Sta. Bull. 132, 1897; Jordan, Jenter and Fuller, F. D., "The food source of milk fat, with studies on the nutrition of milch cows," *Id.*, 197, 1901.

[69] Jones[7].

[70] Kriss, M., and Smith, A. H., "The influence of inorganic salts in the diet on the relative oxidation of carbohydrates and fats," *J. Nut.*, **14**, 487 (1937); **16**, 375 and 385 (1938).

stances, which results in an abnormally low R.Q., or perhaps even in formation of sugar from fat, as in hibernation, shown by an abnormally low R.Q.

Some synthetic reactions may even be endothermic (Chs. 2 and 3); others may be anaerobic when O_2 consumption is not related to heat production. We have the massive heat production of fermentation in the digestive tract, especially of ruminants, which is unrelated to respiratory metabolism or at any rate to O_2 consumption. Catabolism of protein may occur in various ways, oxidative and non-oxidative (Chs. 2, 4). There may be, after all, a great need for more direct calorimetry in combination with indirect, especially for farm animals. In the meantime we do what we can.

Other indirect calorimetric methods might be cited. Thus, if the body weight remains constant over a long period and its composition also remains constant, the heat production may be estimated from the physiological-fuel value of the consumed food. This method is frequently used for estimating energy expenditures and dietary-energy needs in humans.[71]

Fig. 12.26—Photograph (by T. M. Carpenter) of the Benedict-Collins open-circuit chamber for measuring metabolism used in our laboratory (Missouri).

The following example for measuring heat production by difference[72] (on rats) seems to be satisfactory.

Energy of feed consumed	2275.6 Cal
" " feces	171.6 "
" " urine*	75.6 "
" " fat stored	101.0 "
" " protein stored	88.9 "
Heat production by difference	1838.6 "

* 2.1 Cal. were added to the energy of the urine as representing the energy loss during drying (g N loss × 5.447).

Then there are several relations of heat production to various physiological functions, such as ventilation rate, respiration rate, pulse rate (Ch. 24) and the curious one relating metabolism to difference of electrical potential in the skin[73], represented by the equation

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[71] See Atwater, W. O., U. S. Dept. Agr. Farmers Bull. 142, 1901. Atwater and Benedict, F. G., U. S. Dept. Agr. Office of Exper. Stations Bull. 136, 1898–1902. Atwater and Bryant, A. P., "The chemical composition of American food materials." *Id.*, Bull., 28 (rev.), 1906. Forbes, E. B., and Kriss, M., "Revised net-energy values of feeding stuffs for cattle," *J. Agr. Res.*, **31,** 1083 (1925). See also Armsby's, Sherman's and Maynard's books[20, 29], in Ch. 2.

[72] Forbes, E. B., *et al.*, *J. Nut.*, **10,** 461 (1935); **15,** 285 (1938); **18,** 47 (1939).

$$X = \frac{\log Y - \log 0.005}{-0.0396}$$

in which X is the metabolic rate, Y the difference of electrical potential across the specified areas of skin, with the electrodes 12 cm apart.

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[73] Purdy, C., and Sheard, C., *J. Exp. Med.*, **54**, 789 (1931).

Chapter 13

Basal Energy and Protein Metabolism in Relation to Body Weight in Mature Animals of Different Species

> I do not know where or when the various species of animals were given their basal metabolism. Perhaps Noah did it when they left the Ark. I suppose that the reason he could not do a uniform job with the animals was because he did not have scales small enough for the dwarf mice and large enough for the bull and the elephant. *E. F. Du Bois*

13.1: Definitions. *Basal energy metabolism*, also called *post-absorptive metabolism* and *standard metabolism*, is the heat production during complete rest in a thermoneutral environment (Ch. 11) in post-absorptive condition (Ch. 4); it is the resting energy metabolism in a thermoneutral environment uncomplicated by the heat increment of feeding.

As previously explained (Ch. 3), it is doubtful whether much over 25 per cent of the basal metabolism is expended for the work of circulation, respiration, secretion, excretion, and muscle tonus. The work of blood circulation under basal conditions is estimated to account for from 5 to 15 per cent of the total basal metabolism energy; that of the kidney 5 per cent; and that of respiration from 5 to 15 per cent. The remaining basal metabolism energy represents the cost of maintaining the thermodynamically unstable and improbable living state and free-energy losses incidental to the purposeless enzyme activities (analogous to yeast enzymes which continue their catalytic activities after the death of the yeast), and maintaining the characteristic body temperature.

Basal-energy metabolism is a convenient baseline for measuring various energy increments, such as heat increments of muscular work, of feeding, of lactation, of gestation, of keeping warm in cold weather, and the like.

We shall also use the term *resting-energy metabolism* which differs from basal only in that the animal is not in post-absorptive condition.

Endogenous nitrogen excretion is the lowest level of nitrogen excretion attained after an empirically defined time interval (about four days in rat and man) on a low nitrogen but otherwise complete and abundant diet. Endogenous nitrogen excretion, like basal metabolism, is a convenient base for measuring various nitrogen-excretion increments, such as those due to food ingestion.

We shall be concerned mostly with the urinary endogenous nitrogen because of the difficulty of measuring the fecal endogenous nitrogen excretion. The fecal nitrogen is made up of three parts: (1) endogenous or metabolic N, derived from the body; (2) alimentary-lining N, derived from the alimentary lining as a result of "handling" the food; (3) undigested food N. The amount of endogenous fecal nitrogen is profoundly influenced by the dietary roughage and protein. "Protein in direct contact with the mucosa is one of the best stimulants to gastric and intestinal secretions, the residues from which constitute the bulk of 'normal' feces"[1].

Folin[2] demonstrated the presence of two kinds of urinary nitrogen, endogenous and exogenous, in a classic series of papers published in 1905. "I would call the protein metabolism which tends to be constant, *endogenous* metabolism, and the other, the variable protein metabolism, I would call the *exogenous* metabolism". Because of the constancy of the endogenous metabolism he assumed that it represents "an essential part of the activity which distinguishes living cells from dead ones".

Folin demonstrated that the principal end product of the dietary protein disintegration is urea, and the greater the amount of nitrogenous food ingested above the needs, the larger the amount of urea and ammonium salts excreted. The end product of endogenous metabolism apparently least affected by protein ingestion is creatinine. But neutral sulfur and to a less extent uric acid also represent body or endogenous protein metabolism. Urea and creatinine excretion levels, then, represent extremes in the extent to which they are influenced by dietary protein.

Employing isotopic nitrogen to label the amino acids under investigation in metabolism, Schoenheimer[3] found extensive interchange of nitrogen between dietary amino acids and tissue protein, and concluded that "it is scarcely possible to reconcile our findings with any theory which requires a distinction between these two types of nitrogen", referring to endogenous and exogenous nitrogen. However, Burroughs and Mitchell[4] presented evidence substantiating the independence of endogenous and exogenous types of nitrogen metabolism, and attributed the observation of Schoenheimer to the rapid interchange, not in *tissue protein* but in the labile or fluid "deposit protein", which is assumed to rise and fall with the rise and fall of dietary protein.

There are serious difficulties in evaluating endogenous urinary nitrogen because its output varies[5] with (1) duration on N-free diet period prior to commencement of taking the data for evaluation of endogenous N (Fig. 13.19); (2) nature and amount of food intake prior to the experiment; (3) amount of indigestible material in the diet[6].

The endogenous N excretion is evaluated by feeding animals for a given period on practically N-free but otherwise complete diets, or preferably, according to Mitchell[7], on an otherwise nitrogen-free diet containing 4 per cent of whole egg protein.

The apparent endogenous nitrogen level is especially dependent on the length of time the animal is fed on the nitrogen-low diet, and on the nature of this diet. The first effect of such a diet is to depress the food consumption, which upsets the entire nutritional balance. The basic principle of the method is that the animal should consume plentifully a diet which should be complete in every respect, except that it is low in nitrogen.

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[1] Murlin, J. R., and Mattill, H. A., "Value of cereal proteins," *J. Nut.*, **16**, 15 (1938).

[2] Folin, A., "Analyses of thirty '*normal*' urines," *Am. J. Physiol.*, **13**, 45 (1905); "Laws governing the chemical composition of urine," *Id.*, p. 66; "A theory of protein metabolism," *Id.*, p. 117.

[3] Schoenheimer, R., Ratner, S., and Rittenberg, D., *J. Biol. Chem.*, **130**, 703 (1939). Schoenheimer (ed. by H. T. Clarke), "Dynamic state of body constituents," Harvard Univ. Press, 1942.

[4] Burroughs, E. W., Burroughs, H. S., and Mitchell, H. H., *J. Nut.*, **19**, 271 (1940).

[5] Ashworth, U. S., and Brody, S., "Endogenous nitrogen studies," Univ. Missouri Agr. Exp. Sta. Res. Bulls. 189 and 190, 1933, 223 and 228, 1935.

[6] Boas-Fixsen, M. A., "The biological value of protein," *Nut. Abst. and Rev.*, **4**, 447, (1935).

[7] Mitchell, H. H., and Carman, G. G., *J. Biol. Chem.*, **60**, 613 (1924); **68**, 183 (1926).

This chapter is concerned with the relation of basal energy metabolism and urinary endogenous nitrogen excretion to body weight in *mature animals* of *different species* ranging from mice to elephants, with special reference to farm animals. Chapter 14 is concerned with similar relation in *growing animals* of the *same species*, and Chapter 15 with the total maintenance cost in relation to body weight.

13.2: Basal metabolism and the "surface law". A most intriguing observation in basal metabolism studies is that the basal heat production *per unit body weight* in homeotherms decreases rapidly with increasing weight. Thus the basal metabolism *per unit weight* of such small animals as mice and canaries is 20 to 25 times as great as of large animals, such as cattle. This means that the basal-metabolic significance of a physical weight unit in a canary is about 25 times that in a cow. This means that simple body weight is not a suitable reference base for metabolism. The purpose of this section is to discuss critically the reference-base problem in relation to basal energy and protein metabolism. This discussion is based largely on the data in Tables 13.1 and 13.2 (at the end of this chapter), rearranged respectively from our work[8] and Benedict's[9].

According to the laws of Newton and Stefan-Boltzmann (Ch. 11), the rate of cooling of a body is proportional to its surface area. Now if the heat *loss* is proportional to the surfaces, the heat production must likewise be proportional to the surfaces, since in homeotherms heat production must equal heat loss. Homeotherms must, therefore, have developed in the course of evolution a heat-production control to function in proportion to surface area. This, in brief, is the evolutionary logic of the "surface law".

This relation of heat production to linear size and to surface area was first formulated over a century ago by Rameaux and Sarrus[10]. To avoid reviewing many subsequent papers, it seems best to quote, in free translation, somewhat rearranged, this first formulation of the "surface law".

(1) Assuming constancy of body temperature, there must be equality between heat loss and heat production.

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[8] Brody, S., Procter, R. C., and Ashworth, U. S., "Basal metabolism, endogenous nitrogen and neutral sulfur excretions as functions of body weight," Univ. Missouri Agr. Exp. Sta. Res. Bull. 220, pp. 32–33, 1934. Brody and Procter, "Relation between basal metabolism and mature body weight in different species of mammals and birds," *Id.* Res. Bull. 166, 89, 1932.

[9] Benedict, F. G., "Vital energetics, a study in comparative basal mtabolism," Carnegie Inst., Washington Pub., 503, pp. 175–6, 1938.

[10] Sarrus et Rameaux, *Bull. de l'acad. de Med.*, **2,** 538 (1837–8); Rameaux and Sarrus, *Id.*, **3,** (1838–1839). Robiquet and Thillaye, who are sometimes credited with its discovery, merely reported the papers by Rameaux and Sarrus. For a detailed review, see Le Breton, E., *Ann. Physiol. physicochim. biol.*, **2,** 606 (1926).

(2) Assuming equality of other conditions, heat loss is proportional to "free" surface.

(3) Heat production is proportional to oxygen consumption or approximately to inspired air.

(4) Since heat loss and heat production are proportional to "free" surface, and since surfaces vary with the squares of the homologous sides, it follows that oxygen consumption, heat production, and heat loss are proportional to the square of the corresponding dimensions of the animals under comparison.

(5) This proportionality between oxygen consumption and free surface may be achieved in several ways, one of which is by varying the lung surface and number of respirations.

These authors also presented relations between pulse rate, pulse volume, and body size.

The more recent formulations of the "surface law"[11] do not appear to the present reviewer to offer improvements on the original formulation.

In equation form, one may say that surface, or heat loss, or heat production, or oxygen consumption, Y, is proportional to the square of the linear size, L:

$$Y \alpha L^2 \tag{13.1A}$$

or to the $\frac{2}{3}$ power of volume, or to the $\frac{2}{3}$ power of weight, W (if the specific gravity is constant), as indicated by the equation[12]

$$Y = aW^{\frac{2}{3}} \tag{13.1B}$$

or in more general terms

$$Y = aX^b \tag{13.2}$$

We are especially interested (Ch. 24) in what Sarrus and Rameaux had to say concerning the interrelation between oxygen consumption, respiration rate, pulse rate, pulse volume, and body size which anticipate: Hoesslin (1888), Krogh (1916), Henderson (1923), Read (1924), Teissier (1928), and Kleiber (1932) concerning the interrelation of blood flow or oxygen transport (which is proportional to pulse rate and volume per heart beat) and heat production.

[11] See Lusk, G., "The science of nutrition," 1928, and Du Bois, E. F., "Basal metabolism in health and disease", 1936.

[12] Derivations of equation B from A:

Surface area, S, varies with the square of the linear size, L

$$S \alpha L^2$$

Volume or (what is virtually the same) weight, W, varies with the cube of linear size

$$W \alpha L^3$$

or linear size is the cube root of weight

$$L \alpha W^{\frac{1}{3}}$$

and surface area, S, is therefore, the $\frac{2}{3}$ power of weight

$$S \alpha L^2 \alpha (W^{\frac{1}{3}})^2 \alpha W^{\frac{2}{3}}$$

On converting the proportionality to an equality, we have

$$S = aW^{\frac{2}{3}} \tag{13.1B}$$

Thus, according to Kleiber[13], "the influence of body size on metabolism may reasonably be related to oxygen transport" and "if the volume per beat were exactly proportional to the body weight and the pulse rate were exactly proportional to the $\frac{1}{4}$ power of body weight, the intensity of blood flow would be proportional to the $\frac{3}{4}$ power of the body weight". Henderson's results demonstrated a direct proportionality between circulation rate and basal metabolism. An interrelation exists between metabolic rate and pulse rate, and it has been suggested that pulse rate be used for estimating metabolic rate.[14] We are thus indebted to Sarrus and Rameaux not only for originating the "surface law", but also for analyses of the more basic physiologic factors interrelated with metabolism.

Some ten years after the publication of the brief reports by Rameaux and Sarrus, there appeared the widely quoted book by Bergmann[15], who seemed to have formulated the law independently of the French investigators.

Bergmann discussed many problems of more than passing contemporary interest such as: influence of body size (and consequently heat loss and metabolic intensity) on geographic distribution of animals; relative insulating properties of the skin of large and small homeotherms (Bergmann first employed the terms *homeotherm* and *poikilotherm*); possible influence of greater food consumption (by increasing what we now call specific dynamic action) and greater muscular activity (energy cost of work) per unit body weight in small than in large animals, which may assist small homeotherms to maintain their body temperature in spite of greater surface area and consequent greater heat loss.

The development of the Pettenkofer calorimetric method (Ch. 12) and of the Meeh surface-area-measurement method[16] enabled Rubner in Germany, and Richet in France, to substantiate the surface law experimentally. Rubner[17] investigated the law on dogs, and Richet[18] on rabbits.

That heat production must vary with surface area rather than weight *at low temperatures* if small animals are to survive may be illustrated by computations by Kleiber[13], which show that if heat production per unit weight (rather than per unit surface area) were as small in a 60-gram animal as in a

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[13] Hoesslin, H., *Arch. Physiol.*, p. 323 (1888); *Z. Biol.*, **86**, 527 (1927). Krogh, A., "The respiratory exchange of animals and man," 1916. Teissier, G., *Ann. Physiol. physico chim. biol.*, **3**, 212 (1927); **4**, (1928). Read, J. M., *Arch. Int. Med.*, **34**, 553 (1924), and **57**, 521 (1936). Kleiber, M., *Hilgardia*, **6**, 315 (1932). Henderson, Y., *Physiol. Rev.*, **3**, 165 (1923).

[14] Read, J. M., *Arch. Int. Med.*, **34**, 555 (1924). Sutliff, W. D., and Holt, E., *Id.*, **35**, 225 (1925). Murlin, J. R., and Gree, J. R., *Am. J. Physiol.*, **33**, 253 (1914). Winchester, C. F., Mo. Agr. Exp. Sta. Res. Bull., 315, 1940.

[15] Bergmann, H., "Ueber die Vernhältnisse der Wärmeökonomie der Tiere zu ihrer Grosse." Gottingen, 1847-8. Bergmann und Leuckart, R., "Anatomisch—Physiologisch Uebersicht des Tierreiches", Stuttgart, 1852.

[16] Meeh, K., *Z. Biol.*, **15**, 425 (1879).

[17] Rubner, Max, *Z. Biol.*, **19**, 535 (1883); "Die Gesetze des Energie verbrauchs bei der Ernährung", Leipzig and Wien, 1902.

[18] Richet, Ch., *Arch. de physiol.*, **2**, 17, 483 (1890); **3**, 74 (1891).

600-kilogram animal, the small animal could not maintain its temperature in temperate zones without a 20-cm (8-in) insulating cover; small-animal life would be impossible in temperate or frigid zones.

The neatest theoretical derivation of the surface law is due to Teissier[19], who deduced it from the principle of similitude by dimensional analysis. Derivations from the theory of similitude are geometric in the sense that the ratio of the diameter to the circumference of a circle is geometric and constant, regardless of the size of the circle (Ch. 12).

From the theory of similitude, surface area varies with the square of linear size, regardless of size, provided only that the large and small animals are similar in the way that large and small circles are similar. Likewise, power (energy metabolism) varies with the square of linear size regardless of size, provided that the animals are strictly similar and the environmental conditions are strictly homologous[20]. Since both surface area and power are proportional to the square of linear size, or to the $\frac{2}{3}$ power of volume, they are proportional to each other. The surface law is thus arrived at independently of physiologic considerations.

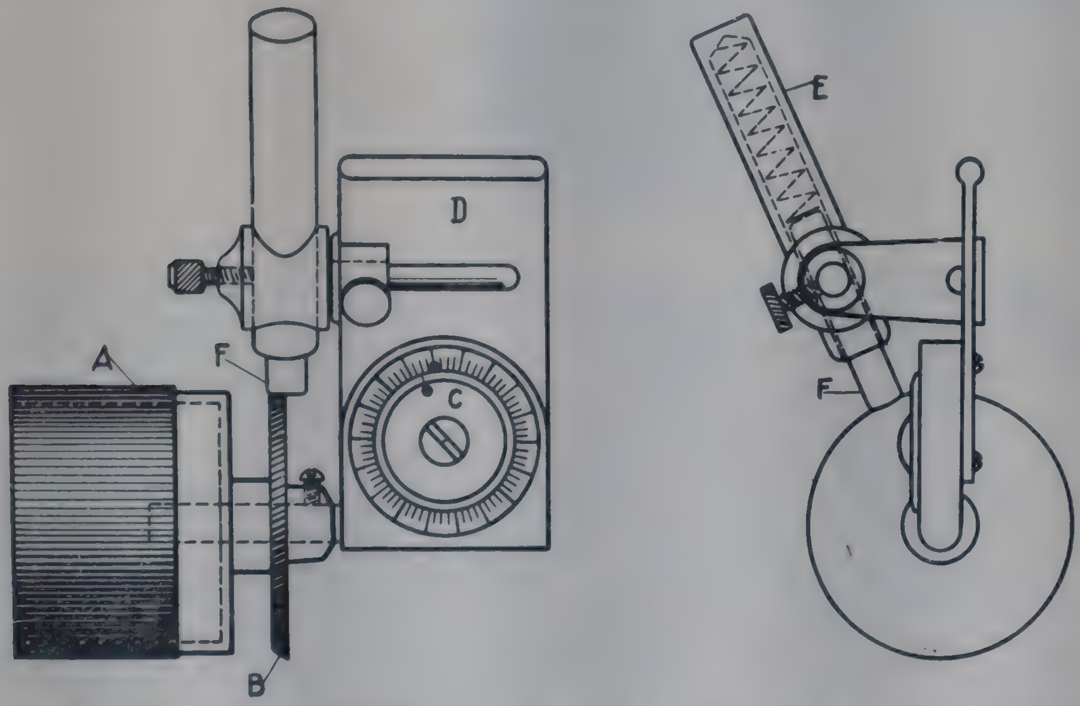

Fig. 13.1a—The surface integrator. The roller A is mounted on an ordinary revolution counter. The crayon is held against the marker by the spring in E.

Since strict biologic similitude between animals in space and time is impossible, strict agreement between observed facts on animals and deductions by dimensional analysis are impossible—only approximations can be made. The magnitude of the surface area and heat production level are interrelated in their common connection with linear size (and other factors, depending on which units we agree to consider as primary and which secondary).

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[19] Teissier, G., "La grandeur de métabolisme en fonction de la taille," *Ann. Physiol. physicochim. biol.*, **4**, 1 (1927). Also Lambert, R., and Teissier, G., Théorie de la similitude biologique," *Id.*, p. 212 (1927).

[20] Homology of environment is obtained at rest in post-absorptive conditions in thermal neutrality, *i.e.*, under "basal conditions".

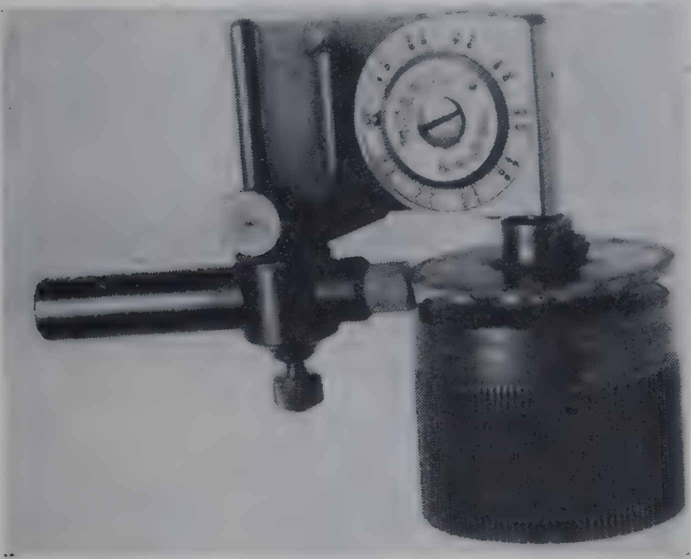

Fig. 13.1b—The surface integrator.

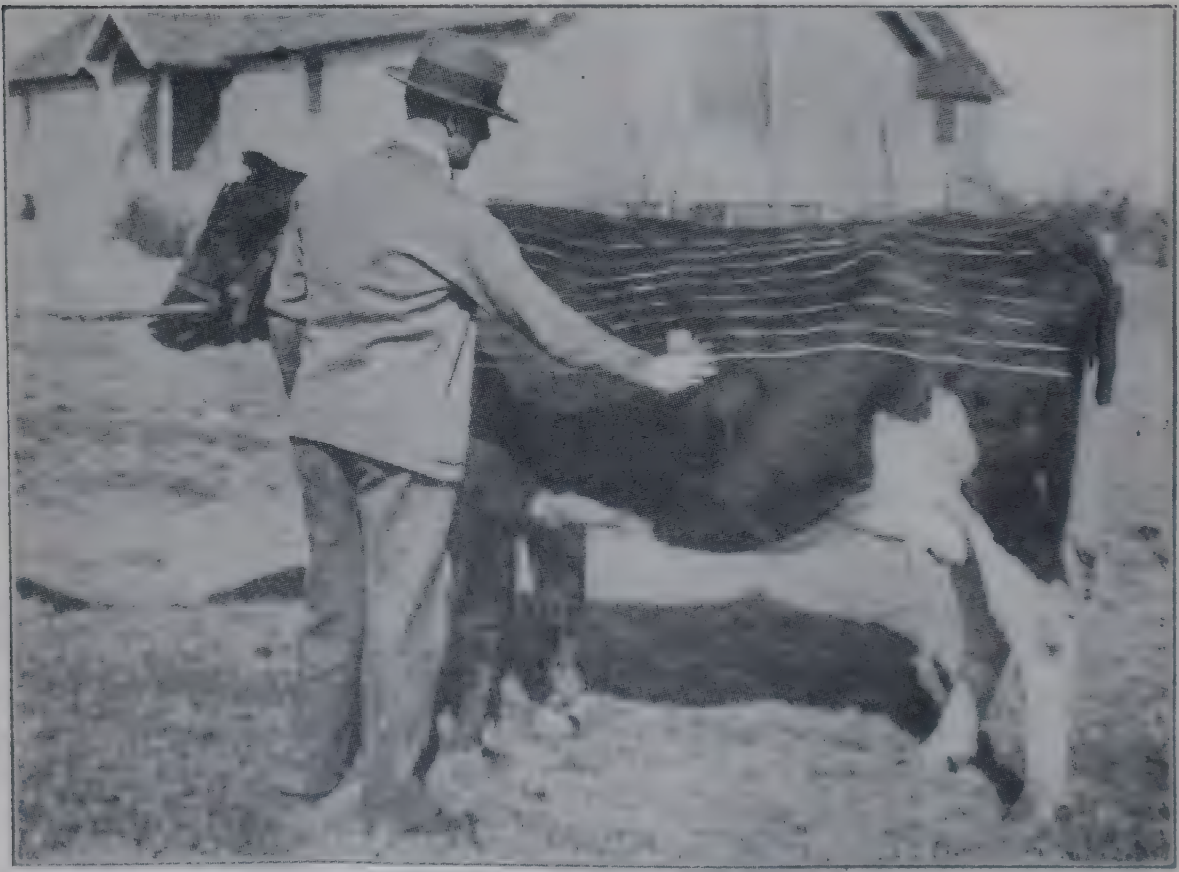

Fig. 13.1c—The surface integrator in action.

The fact that the external *surface area per unit weight* declines with increasing body weight (Fig. 13.2b) probably "explains", from the evolutionary viewpoint—the observation that the *basal metabolism per unit weight* declines with increasing body weight—the fact that the *metabolism per unit weight* in the canary, for example, is about 25 times that of the cow. In the course of evolution only such small animals survived in the colder regions as developed heat-production mechanisms which function in direct proportion to the external surface, in which the ratio of heat production to external surface area is approximately constant.

So much for the remote, or evolutionary, control of the metabolic rate in proportion to external surface rather than to body weight. But what are the *direct mechanisms* which control this relationship, which cause the small animal to metabolize at such a high level per unit weight?

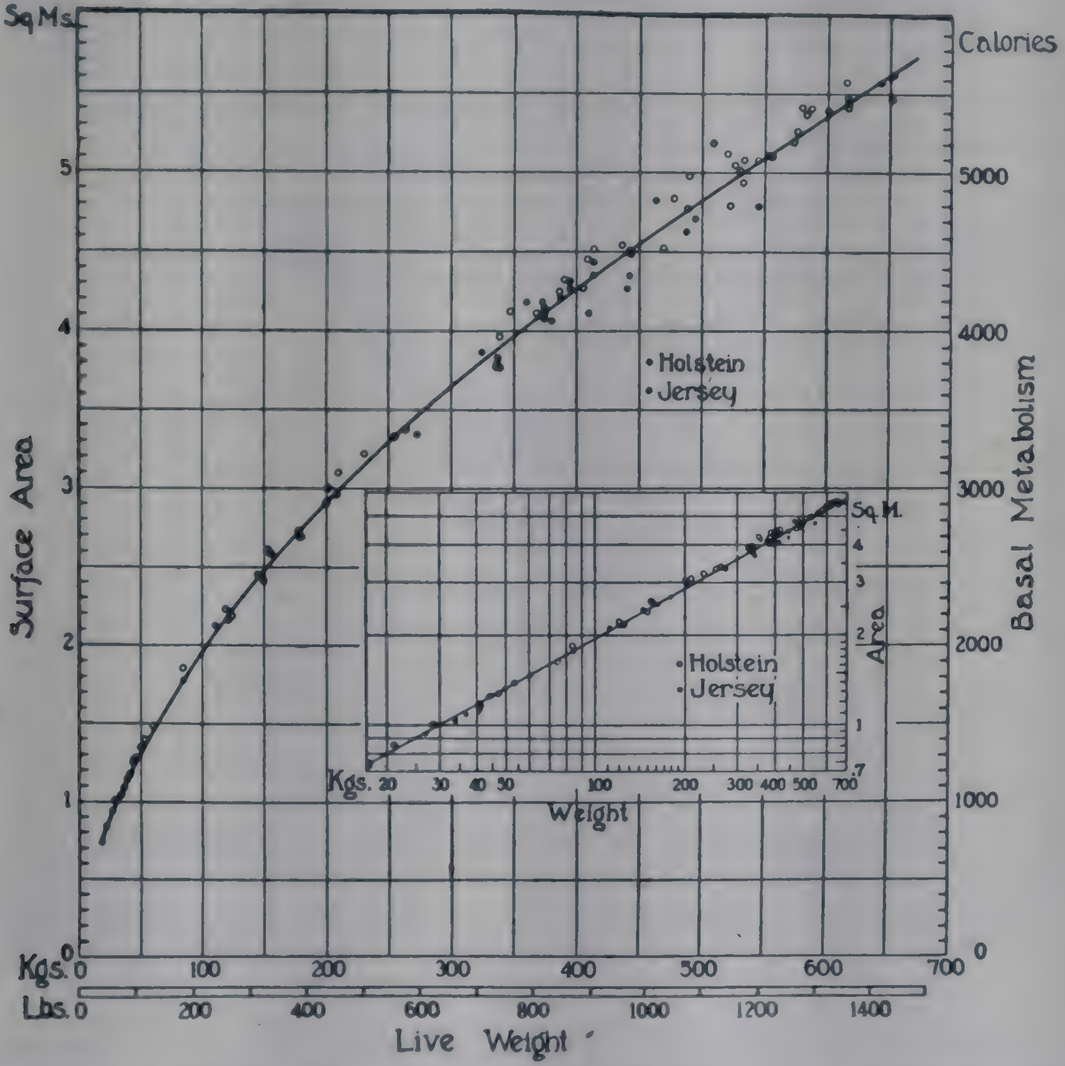

Fig. 13.2a—The surface area, A, is plotted against weight, W, on arithmetic and on logarithmically divided paper. The equation for the data is $A = 0.15\ W^{.56}$ (A in square meters, W in kgs.). See also Fig. 13.2b.

The metabolic intensity is controlled by what Crile called "energy releasing" organs, namely nervous and endocrine systems, especially the brain, pituitary, adrenal, and thyroid glands. Now, it will be presently shown (Ch. 17) that as animals increase in size, the pull of gravity, of course, increases directly with body weight, whereas the strength of the supporting structures, such as of the legs, tend to increase with the $\frac{2}{3}$ power of body weight (with the cross-section *areas* of the supporting structures). Hence, to retain stability, the supporting structures grow more rapidly than the visceral organs, or the visceral organs grow less rapidly than the body as a whole, approximately in proportion to surface area. In brief, the size of the metabolism-controlling organs tends to vary more nearly with surface than with body weight. Since surfaces tend to vary with the $\frac{2}{3}$ power of body weight, with approximately $W^{\frac{2}{3}}$, the *metabolically effective* body size is not simple weight, $W^{1.0}$, but more nearly $W^{\frac{2}{3}}$.

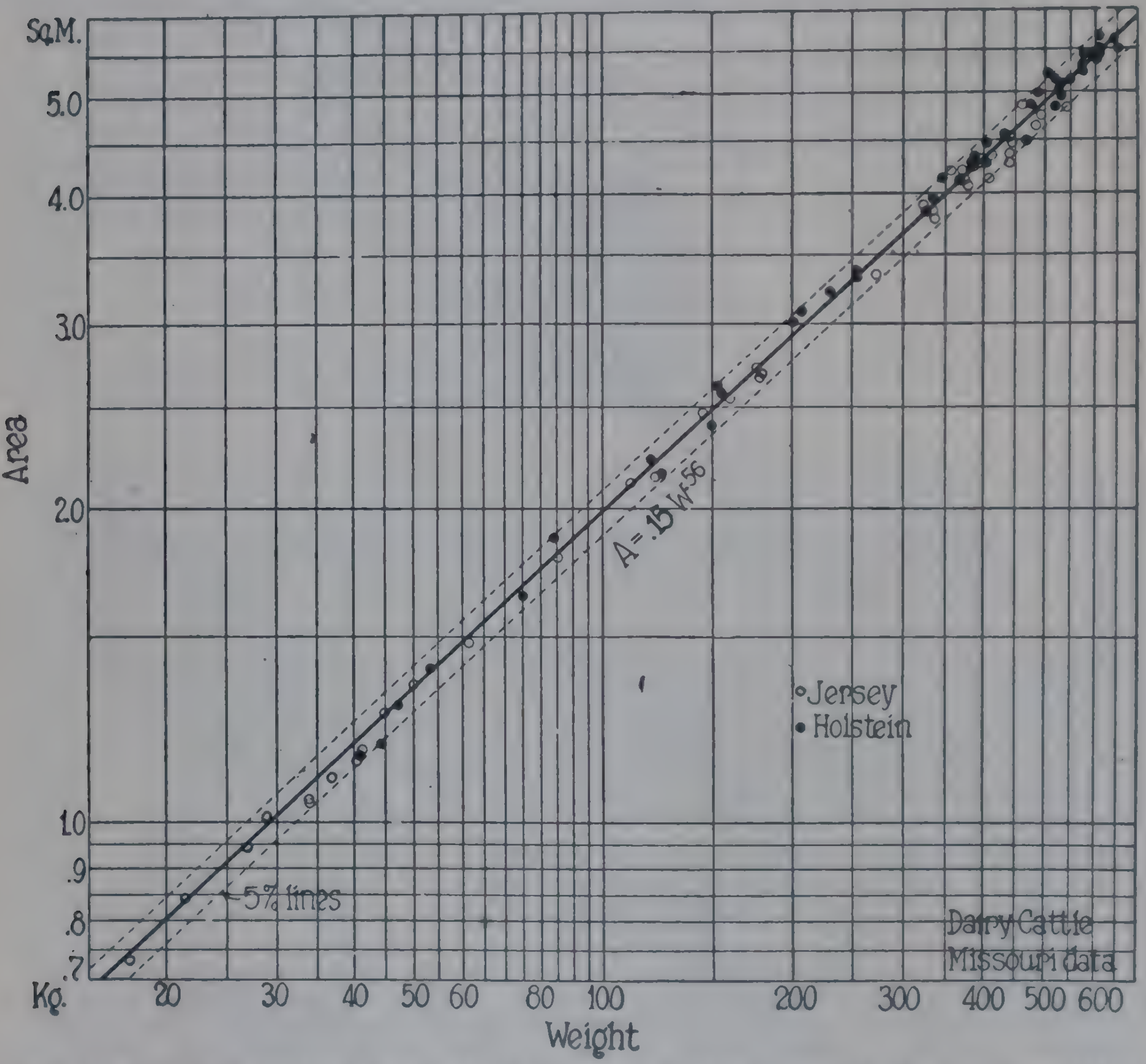

Fig. 13.2b—The surface area, A, is plotted against weight, W, on logarithmically divided paper giving a linear distribution of the data. The equation for the data is $A = 0.15W^{.56}$ (A in square meters, W in kgs.).

13.3: Metabolically effective body size vs. surface area. Since simple weight, $W^{1.0}$, is not a good reference base for basal metabolism, and since metabolism tends to vary more nearly in proportion to surface area or to $W^{\frac{2}{3}}$, shall we then employ surface area or $W^{\frac{2}{3}}$ as reference base? No, for the following reasons:

(1) The surface area of a *living* animal is not constant and cannot be measured in such manner that the results can be checked by different in-

vestigators. Surface-area measurements are not even reproducible on a *dead* animal. Thus, Fig. 13.3 shows a 60 per cent difference in surface area as measured by a similar method by two investigators on dead rats.

(2) Surface area as it relates to heat loss changes with environmental temperature not only by "rolling up" in cold weather and "spreading out" in hot weather, but also by developing heat-conserving and heat-dissipating devices (by varying the fur or feathers, subcutaneous fat, caliber of the blood vessels, and the like), thus changing the *effective* or "free" surface area.

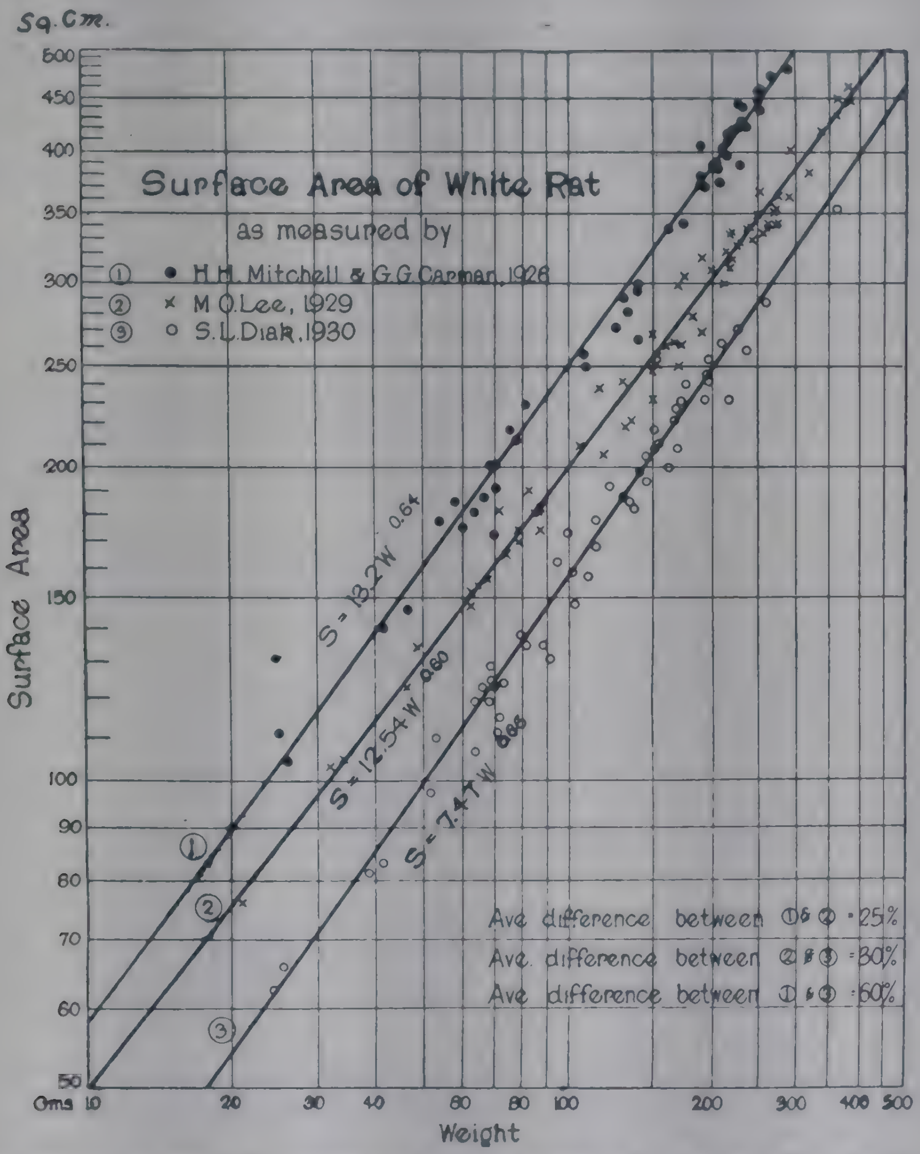

Fig. 13.3—There is a 60% difference in surface area of rats as estimated by Mitchell and by Diak, employing the same general method for estimating area.

(3) It is true that surface area varies with the $\frac{2}{3}$ power of weight, but only in geometrically similar bodies of constant specific gravity; and small and large, young and old, fat and thin, animals—especially of different species—are not geometrically similar and not of constant specific gravity.

(4) Representing metabolism as a function of external surface area would imply that surface area is the "cause" of the metabolic rate, whereas, as ex-

plained above and in other chapters (7, 11, 17), the immediate causative mechanism resides mostly in the neuro-endocrine system and not in the external surface area. Moreover, according to Lambert's "law" of heat radiation, heat loss is proportional not to simple surface but to the profile of the projected area (Sect. 11.5).

For these reasons it would be a gross oversimplification to accept the very vague "surface area" as reference base. The $\frac{2}{3}$ power of weight, $W^{\frac{2}{3}}$, is a more definite reference base than area; but as explained above, there is no geometric reason for assuming that the exponent is exactly $\frac{2}{3}$, since animals are not geometrically similar. It seems more rational, as a matter of principle, to take as reference base not $W^{\frac{2}{3}}$ but W^b the value of the exponent b being determined on the basis of actual data.

As regards actual surface measurements, the data on humans have been compiled by Boyd[21], and on animals by us[22,23].

We measured the surface area of about 600 farm animals by the method[22] illustrated in Figs. 13.1 and 2. It consists in passing a revolving cylinder, attached to a revolution counter, over the surface of the animal. The area is the product of the number of revolutions made by the roller and the area of the roller.

Figs. 13.2 a and b indicate how data on the first group[22] of 96 dairy cattle, ranging in age from birth to maturity, appear when plotted in various ways on logarithmic and also on arithmetic coordinate paper. On the logarithmic paper, the data are distributed beautifully around the straight line, with an average error of only 1.9 per cent, indicating that area is a fractional power function of body weight, as represented by equations (13.2) and (13.3). The numerical value of the exponent is, however, not $\frac{2}{3}$ (*i.e.*, 0.67) but of the order of 0.57. The numerical values of the exponent b of the other animals[23] measured by the integrator method (Fig. 13.1) are shown in Table 13.9.

For comparative purposes we fitted equation (13.2) to human data[23]. The value of the exponent b varied with the range of data employed. When the data range in age from birth to maturity, the value of b in equation (13.2) is of the order of 0.70 (Area $= 0.10W^{0.70}$, weight in kg, area in sq meters). If, however, the data are limited to a narrow age range such as those obtained by Mrs. Bradfield[24] on college girls, the exponent is only 0.55 (Area $= 0.176W^{0.545}$). In other words, form and specific gravity vary with size at *constant age* in a different manner than with changing age during growth.

A similar result was obtained on the relation between surface area and weight of dogs. We found[23] that the value of the exponent b in equation (13.2) is 0.70 for Stewart's dogs, ranging in weight from 0.14 to 4.0 kg; and only 0.37 for Lusk's mature dogs ranging in weight from 6 to 12 kg.

Du Bois[25] suggested that "a tall, thin man may have exactly the same weight as a short, fat man, yet have a much larger surface area", and that there is need to correct for this difference by taking linear size into consideration. This is evident from geometric considerations. The difference in the value of b for humans and for dogs when including wide and narrow age ranges is of the same type as observed by Du Bois on short and tall men. Du Bois' method of including a linear measurement proved to be highly successful for human data and is now generally employed. However, our attempt to include one or several linear measurements for relating area to size of *farm animals* gave disappointing results.

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[21] Boyd, Edith, "The growth of the surface area of the human body", University of Minnesota Press, 1935. For E. F. Du Bois' classic contributions see, "Basal metabolism in health and disease".

[22] Elting, E. C., and Brody, S., "A new method for measuring surface area and its utilization to determine the relation between surface-area growth, weight growth and skeletal growth", Mo. Agr. Exp. Sta. Res. Bull. 89, 1926, Elting, *J. Agr. Res.* **33**, 269 (1926).

[23] Brody, S., Comfort, J. E., and Matthews, J. S., "Further investigations on surface area," Mo. Agr. Exp. Sta. Res. Bull. 115.

[24] Bradfield, H. S., "The determination of the surface area of young women", Mo. Agr. Exp. Sta. Res. Bull. 109.

[25] Du Bois, D., and Du Bois, E. F., *Arch. Int. Med.*, **17**, 863 (1916).

Fig. 13.3 is a graphic argument against adopting surface area as reference base for metabolism. Three groups of rats were measured by the same method, but by different investigators. The curve labelled (1), fitted to the data by Mitchell and Carman[26] is 25 per cent above curve (2), fitted to data by Lee[27]; and curve (2) of Lee is 30 per cent above curve (3), fitted to the data by Diak[28]. No two sets of data agree, and the average difference between two of the sets is 60 per cent.

The above consideration of the surface-area problem leads to the conclusion that while external surface area is a factor in conditioning heat production, it is not logical to employ it as reference base, first because it is difficult to measure with precision the physical (anatomic) surface area, and certainly not the "free" or physiologic surface area—at least of non-human species; and secondly, because the immediate metabolism control resides not in the external surface but in the neuroendocrine system. We have given much space to surface area because of its historic interest, and because its importance is likely to increase in the near future with the accumulation of data on the mechanism of heat dissipation.

In addition to surface area, "active mass" or "protoplasmic mass" has been suggested for use as reference base for metabolism. This suggestion originated with Voit[29], and extended by Benedict[30], Le Breton and Schaeffer[31], and others. The basic idea is that increase in size during growth is associated with increase in the proportion of paraplasm (products of cell differentiation): the ratio nucleus volume/cytoplasm volume or nucleus/cell declines with increasing size during growth of the animal, and that the metabolic rate, as well as growth rate, is conditioned by this ratio.

While much has been written on the active-mass theory, it is practically useless because it is even more difficult to measure "active mass" than surface area in spite of the many published methods[32].

An analysis of published data on purine and total nitrogen in the body in relation to body weight and to heat production yielded much less satisfactory—indeed, very erratic—results than the relation of heat production to surface area.

The foregoing discussions indicate that it is theoretically more logical and practically simpler to relate metabolism, not to surface area or to $W^{\frac{2}{3}}$, or to "active mass", or "protoplasmic mass", but to the noncommittal *physiologically effective* body size represented symbolically by W^b, the value of the exponent b to be determined from actual data. The ratio of metabolism, Y, to

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[26] Mitchell, H. H., and Carman, G. G., *Am. J. Physiol.*, **76**, 380 (1926).

[27] Lee, M. O., *Am. J. Physiol.*, **89**, 24 (1929).

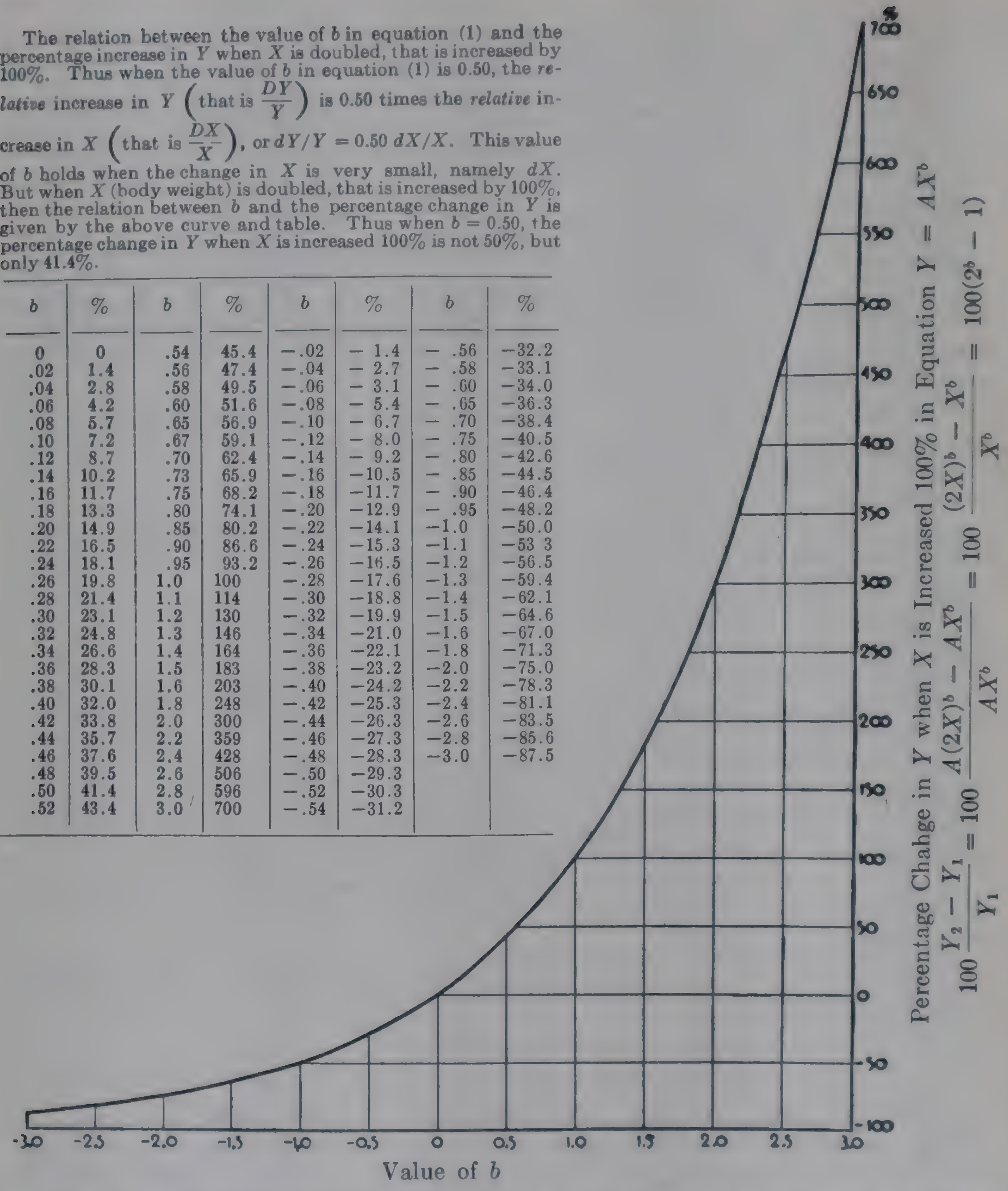
[28] Diak, S. L., *J. Nut.*, **3**, 289 (1930).

[29] Voit, C., *Z. Biol.*, **41**, 113 (1901).

[30] *Cf.* Benedict, F. G., *J. Biol. Chem.*, **20**, 263 (1915); *Am. J. Physiol.*, **41**, 292 (1916); and many subsequent papers.

[31] Le Breton and Schaeffer, G., "Récherches de physiologie générale sur la determination de la masse protoplasmique active," Trav. de l'Institut de Physiol., Paris, 1923.

[32] *Cf.* Conklin, E. G., *J. Exp. Zool.*, **12**, 1 (1912); Mathews, A. P., *Am. J. Physiol.*, **1**, 445 (1898); Robertson, T. B., *Australian J. Exp. Biol. Med. Sci.*, **6**, 33 (1929). Robertson and Dawborn, M. C., *Id.*, p. 261. Huelin, F. E., *Id.*, p. 59; Marston, H. R., *Id.*, **1**, 99 (1924). Le Breton and Schaeffer, "Variation Biochim." etc.[31]



The relation between the value of b in equation (1) and the percentage increase in Y when X is doubled, that is increased by 100%. Thus when the value of b in equation (1) is 0.50, the *relative* increase in Y $\left(\text{that is } \frac{DY}{Y}\right)$ is 0.50 times the *relative* increase in X $\left(\text{that is } \frac{DX}{X}\right)$, or $dY/Y = 0.50\ dX/X$. This value of b holds when the change in X is very small, namely dX. But when X (body weight) is doubled, that is increased by 100%, then the relation between b and the percentage change in Y is given by the above curve and table. Thus when $b = 0.50$, the percentage change in Y when X is increased 100% is not 50%, but only 41.4%.

b	%	b	%	b	%	b	%
0	0	.54	45.4	−.02	− 1.4	− .56	−32.2
.02	1.4	.56	47.4	−.04	− 2.7	− .58	−33.1
.04	2.8	.58	49.5	−.06	− 3.1	− .60	−34.0
.06	4.2	.60	51.6	−.08	− 5.4	− .65	−36.3
.08	5.7	.65	56.9	−.10	− 6.7	− .70	−38.4
.10	7.2	.67	59.1	−.12	− 8.0	− .75	−40.5
.12	8.7	.70	62.4	−.14	− 9.2	− .80	−42.6
.14	10.2	.73	65.9	−.16	−10.5	− .85	−44.5
.16	11.7	.75	68.2	−.18	−11.7	− .90	−46.4
.18	13.3	.80	74.1	−.20	−12.9	− .95	−48.2
.20	14.9	.85	80.2	−.22	−14.1	−1.0	−50.0
.22	16.5	.90	86.6	−.24	−15.3	−1.1	−53 3
.24	18.1	.95	93.2	−.26	−16.5	−1.2	−56.5
.26	19.8	1.0	100	−.28	−17.6	−1.3	−59.4
.28	21.4	1.1	114	−.30	−18.8	−1.4	−62.1
.30	23.1	1.2	130	−.32	−19.9	−1.5	−64.6
.32	24.8	1.3	146	−.34	−21.0	−1.6	−67.0
.34	26.6	1.4	164	−.36	−22.1	−1.8	−71.3
.36	28.3	1.5	183	−.38	−23.2	−2.0	−75.0
.38	30.1	1.6	203	−.40	−24.2	−2.2	−78.3
.40	32.0	1.8	248	−.42	−25.3	−2.4	−81.1
.42	33.8	2.0	300	−.44	−26.3	−2.6	−83.5
.44	35.7	2.2	359	−.46	−27.3	−2.8	−85.6
.46	37.6	2.4	428	−.48	−28.3	−3.0	−87.5
.48	39.5	2.6	506	−.50	−29.3		
.50	41.4	2.8	596	−.52	−30.3		
.52	43.4	3.0	700	−.54	−31.2		

Fig. 13.4—The relation between the value of b in the equation $Y = aX^b$ or $Y = aW^b$ and the percentage change in Y when X or W is doubled. Derivation of equation relating percentage change with the exponent b: Let $Y_1 = aX^b$, and $Y_2 = aX^b$; therefore the increase in Y expressed in per cent of Y_1 is $100 \frac{Y_2 - Y_1}{Y_1} = 100X \frac{aX_2^b - aX_1^b}{aX_1^b} = 100 \frac{X_2^b - X_1^b}{X_1^b} = 100 \left(\frac{X_2}{X_1}\right)^b - 100$. When X_2 is twice X_1, $X_2 = 2X_1$, and percentage change is given by $100 \left(\frac{2X_1}{X_1}\right)^b - 100 = 100(2^b - 1)$.

metabolically effective body size, W^b, or to X^b, should be approximately constant, a.

$$\frac{Y}{W^b} = a; \quad \text{or} \quad \frac{Y}{X^b} = a \tag{13.2}$$

13.4: Properties of equations $Y = aX^b$ *and* $Y = aX^bH^m$ relating surface area or metabolism to body size. A brief discussion of the mathematical significance of equation (13.2) above may be helpful at this time.

This equation is usually written in the form

$$Y = aX^b \tag{13.2}$$

in which Y is metabolism, surface area, or other given dependent variable, and X is body weight or other independent variable.

This equation is generally known as a parabola, or a logarithmic equation, since on taking logarithms we obtain the equation

$$\log Y = \log a + b \log X \tag{13.3}$$

which, incidentally, has the same *form* as the linear equation

$$Y = a + bX \tag{13.4}$$

In fitting the logarithmic equation, (13.3) to data, exactly the same method is used as in fitting the linear equation (13.4), except that in place of Y or X we deal with log Y and log X.

Just as linear equation (13.4) is a straight line on arithmetic paper, so logarithmic equation (13.3) is a straight line on logarithmic paper. As linear equation (13.4) represents constant *absolute* increase in Y for constant *absolute* increase in X, so logarithmic equation (13.3) represents constant *percentage* increase in Y for constant *percentage* increase in X. This is the feature of logarithmic coordinate paper: deviations from the average are shown spatially in proportion not to *absolute* but to *percentage* deviation. Thus a 10-lb deviation on a 100-lb animal is shown on logarithmic paper by the same distance as a 100-lb deviation on a 1000-lb animal, because in both cases the *percentage* deviation is the same. For practical purposes it is more useful to have data or tables of constant *percentage* than of constant *absolute* accuracy. The linear equation (13.4) is fitted to data by the method of least squares, on the assumption that a given *absolute* deviation about the fitted line is equally important to animals of different weight; the logarithmic equation (13.3) is fitted to data on the assumption that a given *percentage* deviation about the fitted line is equally important to animals of different size. It is obviously more rational to assume that a given *percentage* deviation has the same significance for the large as for the small animal, than that a given *absolute* deviation has the same significance for the large as for the small animal.

Equation (13.2) is interpreted as meaning that increasing X by 1 per cent is associated with a differential increase in Y by b per cent. Thus, assuming that in equation (13.2), Y represents metabolism or surface area and X represents body weight and the value of the exponent b is 0.7, then increasing body weight by 1 per cent is associated with a differential increase in metabolism or in area by 0.7 per cent; doubling body weight (increasing it by 100 per cent) is associated with a metabolic or area increase not of 100 per cent but of 70 per cent.

The value of the exponent represents *differential* or *very small* relative change as computed by the differential calculus. The relation between the differentially computed and conventionally computed changes is indicated in Fig. 13.4.

The exponent is the actual slope of the curve when plotted on logarithmic coordinate paper; it is the ratio $\frac{Y_1 - Y_2}{X_1 - X_2}$, which, if desired, can be measured by a pair of dividers, "by inspection", or by the method of least squares, as illustrated in the appendix to this chapter.

Instead of relating Y (metabolism, area, etc.) to weight alone, W^b or X^b, we may include another independent variable such as height, H^m. Du Bois[25] reasoned that since area is a bidimensional measurement, both sides of the equation relating area to size should be bidimensional. In order to keep the formula containing weight and height bidimensional, it was written in the form

$$A = CW^{1/a}H^{1/b}$$

and by trial the values of a and b were found that keep the form bidimensional. In this way it was found that the formula

$$A = 71.8W^{.425}H^{.725}$$

is bidimensional[33] and best represents the data. This is the well-known Du Bois height-weight or linear formula for estimating surface area of humans.

Cowgill and Drabkin[34], working with dogs, concluded that the value of m, that is, the exponent of H in the Du Bois formula, is not 0.725, but 1.0.

All the above mentioned relations between surface area and body size may be represented by the equation

$$A = aH^mW^n$$

According to the general assumption that weight varies with the $\frac{2}{3}$ power of body weight, the value of m is zero; according to Cowgill and Drabkin's formula, it is 1; according to Du Bois formula, it is 0.725.

What is the value of m? Is it 0, 1, or 0.725?

The answer may be formulated graphically as follows:

Equation (13.2)

$$A = aW^b \tag{13.2}$$

is changed to

$$A = aW^bH^m \tag{13.2A}$$

in which A is area, W is weight, H is height.

Then

$$\frac{A}{H^m} = aW^b \tag{13.2B}$$

and, on taking logarithms,

$$\log \frac{A}{H^m} = \log a + b \log W \tag{13.2C}$$

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[33] Example of bidimensional writing of the area formula: Dimensionally, area, A, is height squared, H^2, and weight is height cubed, H^3; height is the cube root of weight, $W^{\frac{1}{3}}$, so that

$$A = W^{.425}H^{.725}$$

may be written dimensionally

$$\begin{aligned} H^2 &= H^{3 \times .425}H^{.725} \\ &= H^{1.275}H^{.725} \\ \therefore H^2 &= H^2 \end{aligned}$$

[34] Cowgill, G. R., and Drabkin, D. L., *Am. J. Physiol.*, **81**, 36 (1927).

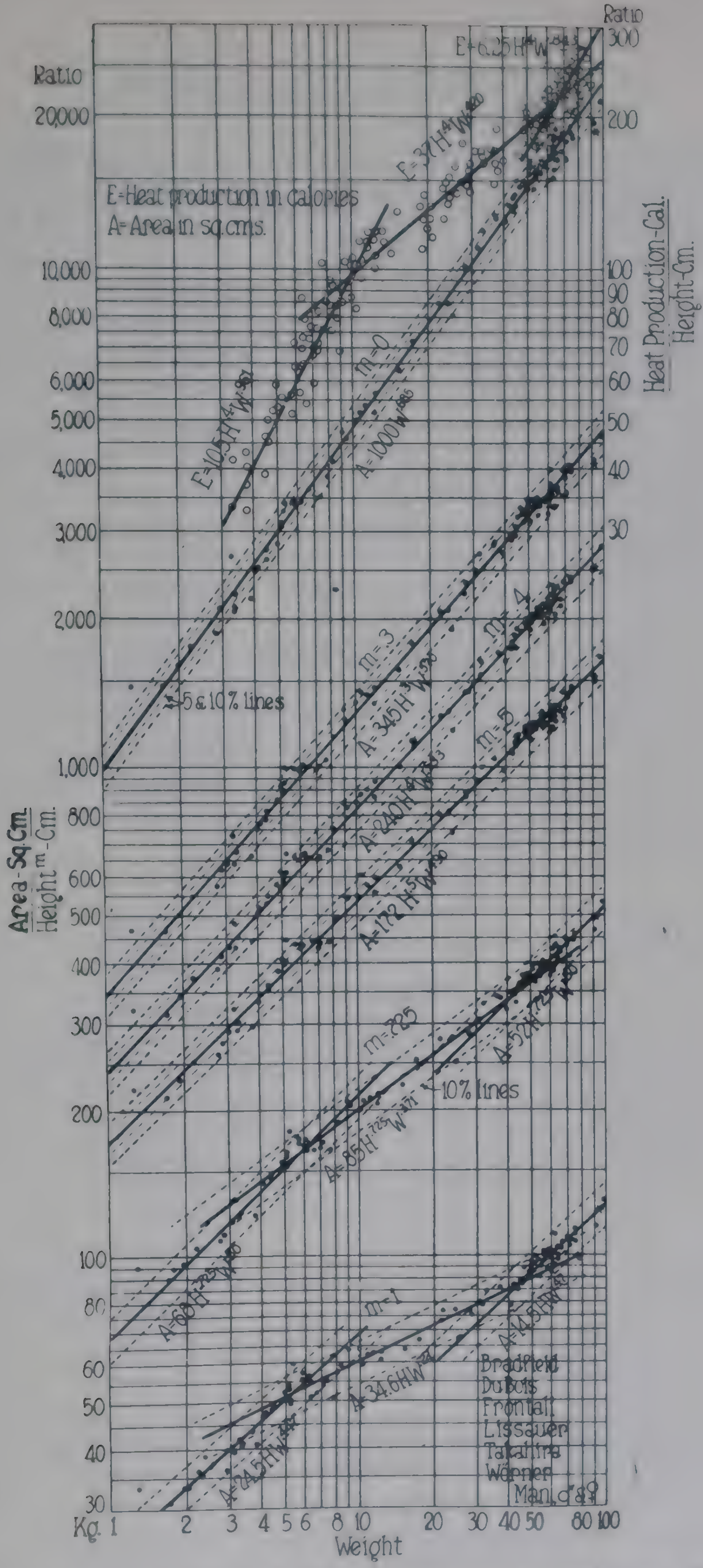

Fig. 13.5 –The relation of area, A, and of basal energy metabolism, E, to body weight, W, and height, H, in man. The ratios $\frac{A}{H^m}$ are plotted against weight. The most nearly straight line is obtained when m is 0.4. On increasing the value of m the resulting curve tends to break up into 3 segments. The breaks are distinct when $m = 1$ (value employed by Cowgill and Drabkin for dogs), or 0.725 (value employed by Du Bois and Du Bois for man). The star represents Mrs. McK (see Du Bois and Du Bois) weighing 204 lbs and having the height of a 12-year old girl. Note the position of the star for various values of the exponent m. Note that when $m = 0$, that is, when height is omitted, the distribution of the metabolism data is satisfactorily linear, with a slope (value of b) of 0.685.

which indicates that plotting logarithms of the ratios of area to height, raised to the power m, against the logarithms of weight, should give a straight line of slope b. Fig. 13.5 represents such ratios for human surface-weight data from birth to maturity.

The lowest curve in Fig. 13.5 represents the ratios of area to simple height, to $H^{1.0}$, plotted against weight on a logarithmic grid (equivalent to plotting $\log A/H$ against $\log W$). The curve is seen to be made up of three fairly distinct segments. The equations for each of the three segments are given on the curve. According to equation (13.2C), the plot of $\log A/H$ against W should result in a straight line while Fig. 13.5 shows that it is not a straight line; therefore, either equation (13.2C) does not represent the data, or the value of m is not 1; in other words, this curve precludes the value of m being unity, 1.0, as assumed by Cowgill and Drabkin[34] for dogs.

The second curve from the bottom represents a similar plot when m is assumed to be 0.725, the value assumed by Du Bois and Du Bois[25] for man. When the value of m is 0.725, the distribution of the data points more nearly approaches a straight line.

In similar manner we assumed the value of m to be 0.5, 0.4, 0.3, and 0, and the resulting values of A/H^m were plotted against W. Looking over the chart we concluded by *inspection* that the best agreement between observed and computed values is obtained when $m = 0.4$. We included in these computations the data by Bradfield[24], Du Bois and Du Bois[35], Frontali[36], Lissauer[37], Takahira[38], and Wörner[39], a total of 133 measurements, and with two exceptions, all the data points are within 10 per cent of the average.

The results in Fig. 13.5 lead to the conclusion that for individuals of "normal" build the equation relating area to weight and to height is

$$A = 240\ H^{.40}W^{.53} \tag{13.5}$$

contrasted to Du Bois'

$$A = 71.84\ H^{.725}W^{.425}$$

in which A is surface area in square centimeters, H height in centimeters, and W weight in kilograms. Equation (13.5) was used in preparing Fig. 13.6 for predicting surface area from weight and height in man.

But for individuals of "normal" build it is not really necessary to take height into consideration, because as shown in the top curve of Fig. 13.5 the equation

$$A = 1000W^{.685}$$

is satisfactory.

As previously noted, introducing a linear measurement in the formula does not improve its predictability for *farm animals*, although it does so remarkably well for man. The age-weight-height interrelation for man is of quite a different order than for farm animals (Chs. 16 and 17).

13.5: Relation of basal energy metabolism to body weight in mature animals of different species. The metabolism data from mice to elephants in Table 13.1 were plotted on logarithmic coordinate paper and equation (13.2) fitted by the method of least squares. The result is shown in Fig. 13.7. The value of b, the slope of the curve on the logarithmic paper, is 0.73, meaning that doubling body weight is associated with a differential metabolic increase

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[35] Du Bois, D., and Du Bois, E. F., *Arch. Int. Med.*, **15**, 868 (1915); **17**, 863 (1916).

[36] Frontali, G., *Rivista di clinica Pediatrica*, **25**, 241 (1927).

[37] Lissauer, W., *Jahrb. Kinderh.*, **58**, 392 (1903).

[38] Takahira, H., Report of the Imperial Government Institution for Nutrition, Tokyo, Vol. I, No. 1, paper II, pp. 125–27, 1924.

[39] Wörner, H., *Z. Gesammt. Exper. Med.*, **33**, 510 (1923).

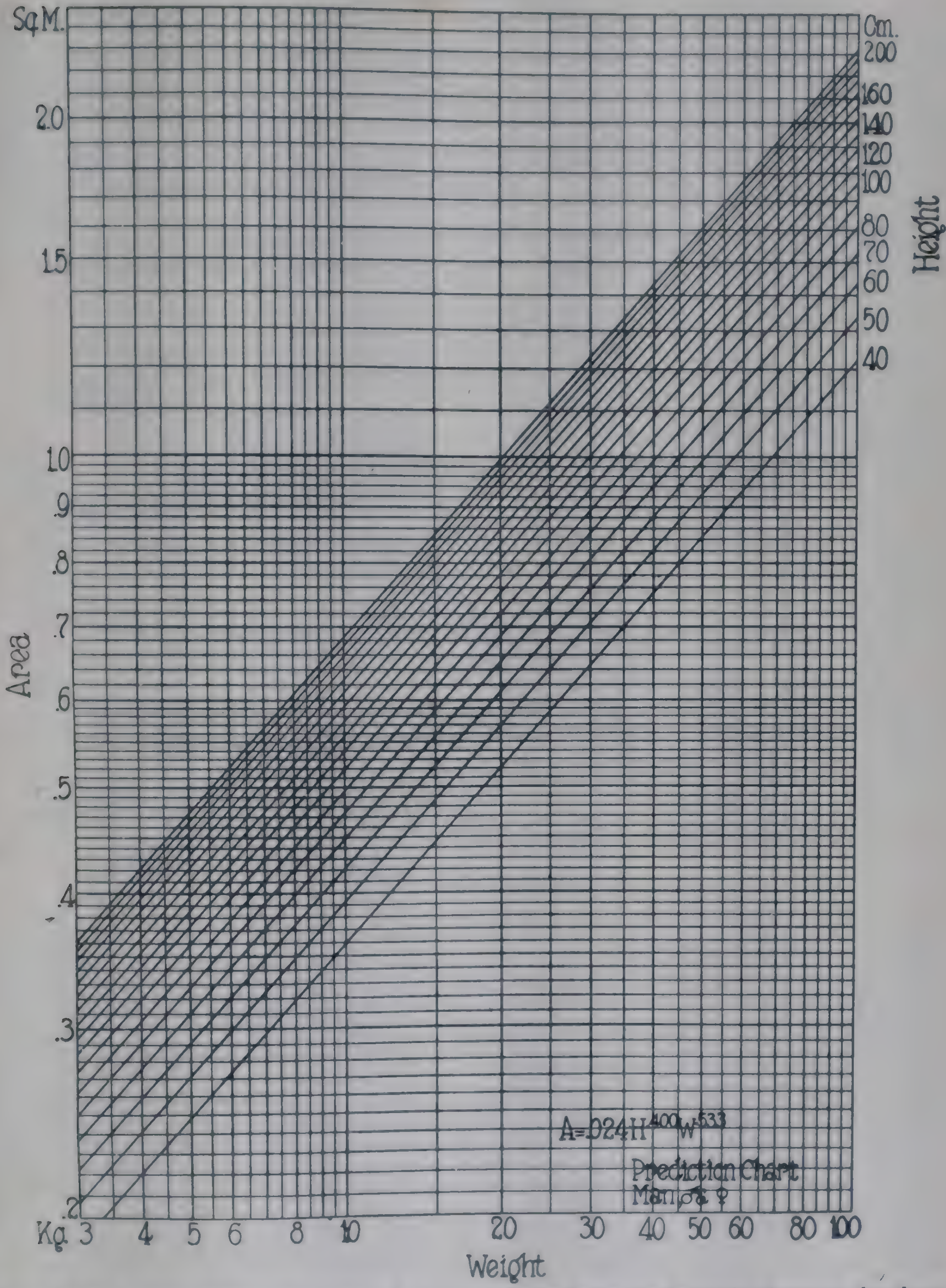

Fig. 13.6—A chart for estimating surface area of man from the formula given on the chart.

of 73 per cent. The average numerical value of the ratio $\frac{\text{Cal/24 hours}}{\text{kg}^{0.73}}$ is 70.5, meaning that the average basal metabolism of the animals is 70.5 Cal per 24 hours per $\text{kg}^{0.73}$. The deviations from the average are given for each value in Table 13.1.

Benedict[40], criticized this result because the metabolism of the dwarf mouse, marmot, boar, bull, and elephant deviate considerably from this average (Table 13.2). Our reply is that the metabolism values for these animals represent special cases. The dwarf mouse is a hypopituitary and a hypothyroid animal (this is the reason for its dwarf size); it lacks normal metabolic mechanisms. The marmot is a hibernating animal, bordering between homeothermy and poikilothermy (its rectal temperature may drop to 3° C during hibernation). In other words, the unusually low metabolism per kg$^{0.73}$ for the marmot is a species characteristic, not due to *size as such*. The high values for the boar, bull and elephant reflect technical difficulties in measuring metabolism of these temperamental animals. At any rate, the deviations do not appear to be due to *size as such* but to other factors, and all we claim is that the ratio of metabolism to the 0.73 power of weight is independent of body size *as such*: while the metabolism per kilo changes *systematically* from 8 Cal/kg for the elephant to 200 Cal/Kg for the mouse; the metab-

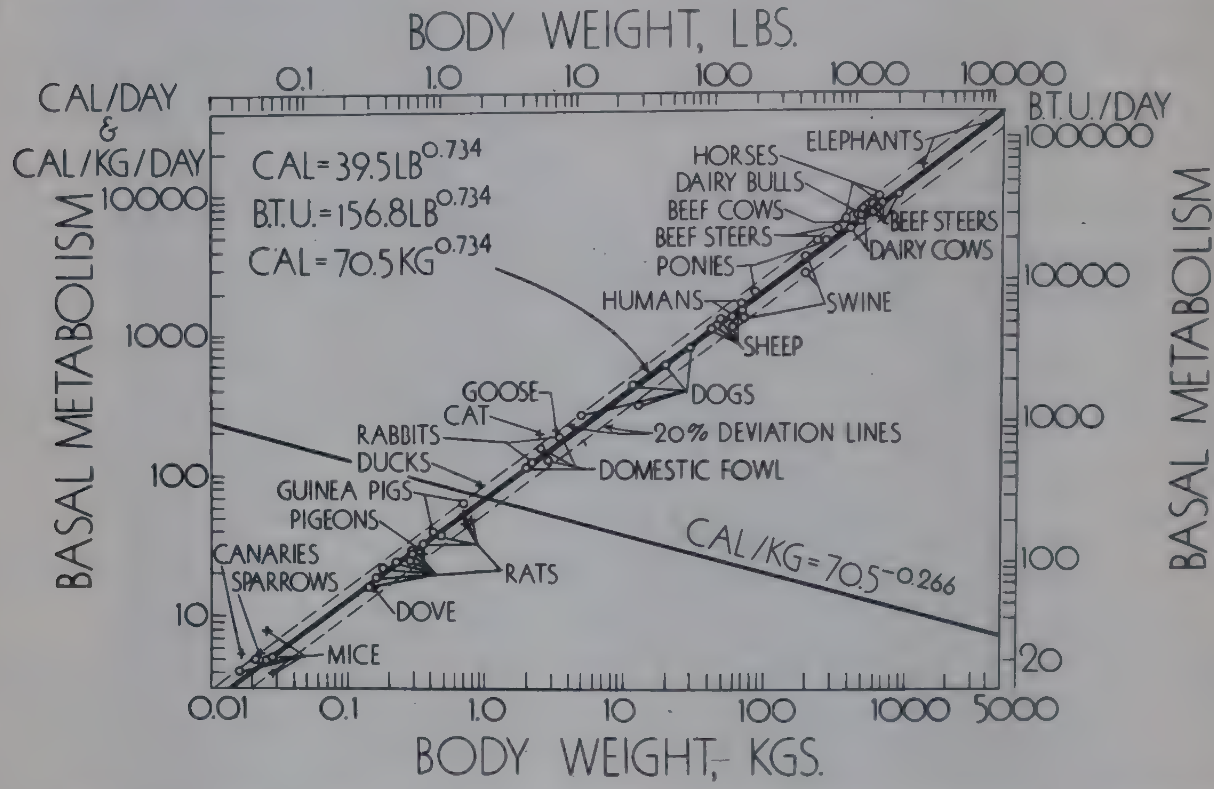

Fig. 13.7—Basal metabolism of mature animals of different species, from mice to elephants, plotted against body weight on a double-logarithmic grid. The rising curve represents metabolism per animal per day; the declininc curve represents the metaboism per kg body weight per day, both plotted against body weight. The rising curve is represented by the equation Cal = 70.5 kg$^{0.734}$ or Cal/Kg$^{0.734}$ = 70.5. The declining curve has the equation Cal/kg = 70.5 kg$^{-0.266}$. (Note error in the equation on the declining curve in the chart—the kg was omitted by oversight.) The sum of the exponents of the rising and declining curves is 1.0 (0.734 + 0.266 = 1.0). The data represented by the crosses were omitted in computing the equation. The numerical data are given in Table 13.1, page 388–389. The slope of the rising curve, 0.73, means that an increase in body weight of 100 per cent is associated with an increase in basal metabolism of about 73 per cent. Note the consistent distribution of the data about the straight line.

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[40] Benedict,[9] and Table 13.2.

olism per $Kg^{0.73}$ shows no *systematic* change with changing body weight. This is as true for Benedict's data, Table 13.2, as for the data in Table 13.1.

Fig. 13.8 shows that the metabolism of mature *birds* of different species varies more nearly with the $\frac{2}{3}$ power of body weight than with the 0.73 power, as appears to be the case with mammals.

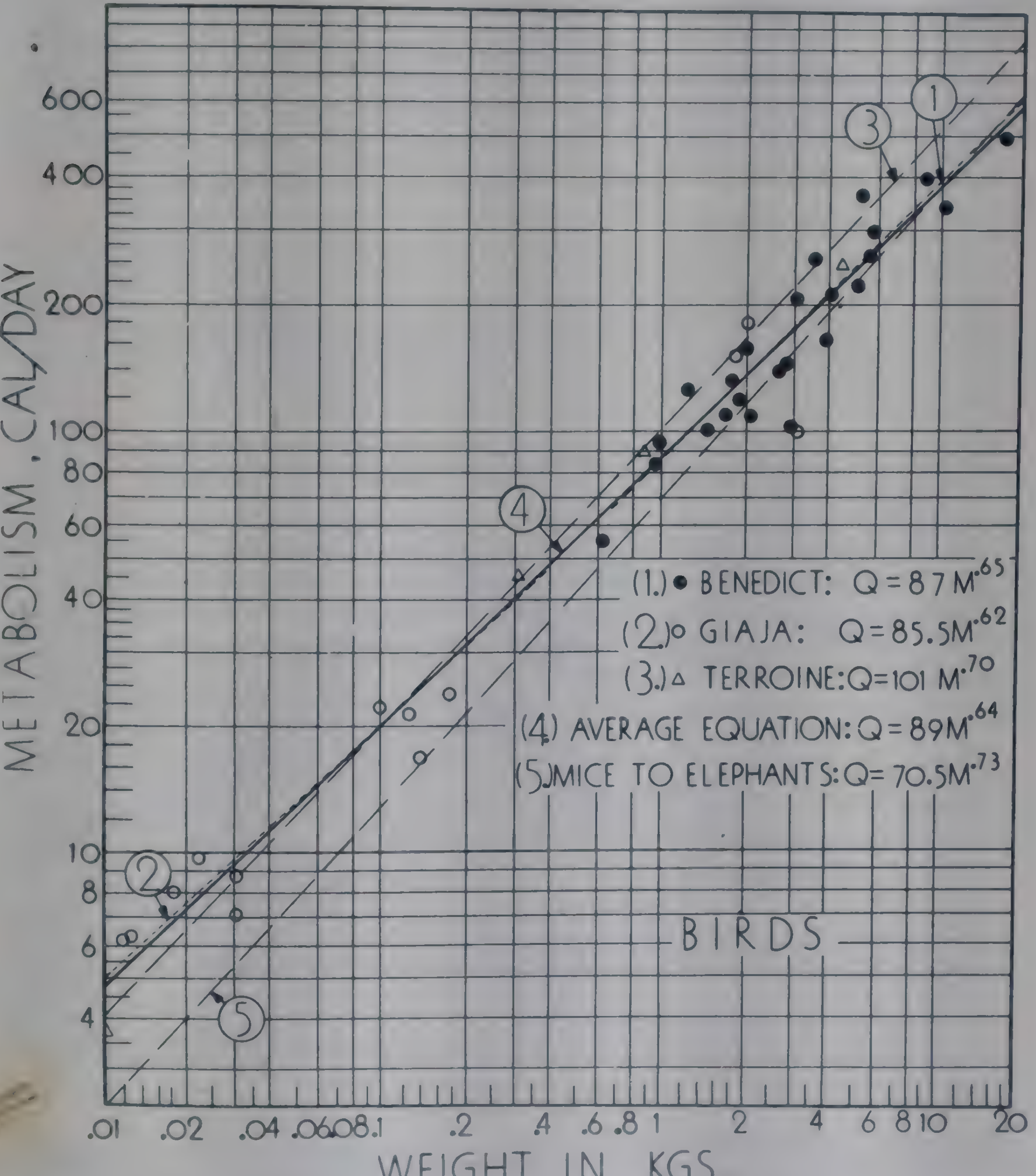

Fig. 13.8—Basal metabolism of mature birds of different species plotted from data by the authors indicated in the charts.

Fig. 13.9 compares the metabolism of individual *growing* animals with the average curve in Fig. 13.7 for *mature* animals of *different species*. The deviations are so great that we decided to devote a special chapter (14) to the relation of metabolism to weight in the same growing animals.

Fig. 13.7 shows that the numerical value of a of the ratio $\frac{\text{Cal/day}}{\text{kg}^{0.73}}$, varies with the units employed. It is 70.5 when weight is in kg and heat in Cal/24 hours; 39.5 when weight is in pounds and heat in kilograms; and 156.8 when weight is in pounds and heat is in Btu.

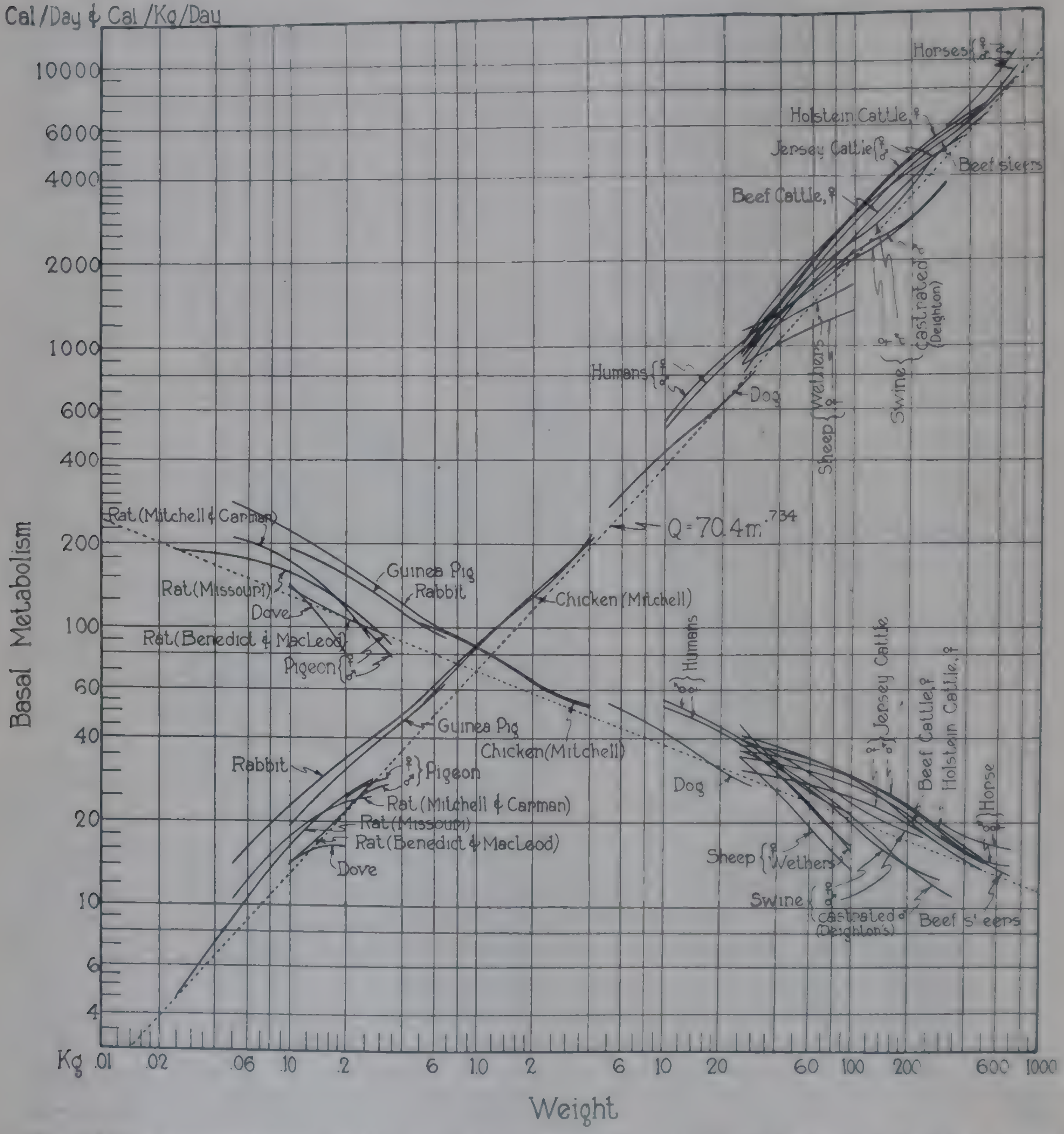

Fig. 13.9—A comparison of the weight curves of metabolism of growing animals with the broken curve of the equation $Q = 70.5M^{.73}$. The declining curves represent metabolism per kg as compared to the declining broken curve from Fig. 13.7, namely $Q = 70.5M^{-0.27}$.

As previously explained, over a century ago Sarrus and Rameaux suggested that either surface area or the square of linear size or, what amounts to the same, the $\frac{2}{3}$ power of weight be used as reference base for heat production and dissipation.

In 1916 Krogh[41] suggested the use of a power of weight as reference base. In 1932

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[41] Krogh, A., "The respiratory exchange of animals and man," New York, 1916.

Kleiber[42] reported that the $\frac{3}{4}$ power of weight is a good reference base. At about the same, employing a different method of analysis and different data, we published[43] our results reporting the 0.73 power of weight as reference base. This report was extended[44] in 1934, demonstrating that not only basal energy, but also endogenous nitrogen and neutral sulfur tend to vary with the 0.73 power of body weight. The Conference on Energy Metabolism[45] tentatively adopted the 0.73 power of body weight as reference base for energy metabolism. Benedict[46] criticized this reference base on the ground that the metabolism of the dwarf mouse, marmot, bear, bull, and elephant deviated grossly from the predicted values (see Table 13.2).

As further argument against using the 0.73 power of body weight as reference base, Lee[47] reported that a linear equation (13.4) represented metabolism data on rabbits as well as a power equation (13.2). However, Lee's equation

$$Y = 39.5X + 22.5$$

shows it to be irrational because extrapolation gives a metabolism of 22.5 Cal/hr for zero body weight. We worked over Lee's data with the result shown in Fig. 13.10, on a logarithmic grid in the upper left and on an arithmetic grid on the lower right corner. It appears that for the given range of data there is not much difference between the arithmetic and logarithmic fit; the slope of the logarithmic line is 0.82 rather than 0.73, as in Fig. 13.7.

To check further the question as to whether within the species a linear equation is as good as a logarithmic, we measured[48] the basal metabolism of four groups of mature Rhode Island Red fowls, normal, and bantam (small) varieties. The result in Fig. 13.11 shows that, if both varieties are included, the fowl curve coincides with the general mammalian curve in Fig. 13.7; the slope range for the various groups is from 0.70 to 0.74, and they practically coincide with curve (3), representing the mouse-to-elephant curve in Fig. 13.7. If, however, the equation is fitted to the larger variety alone (omitting the bantams) the slope is very low, 0.30 to 0.54, perhaps due to the fact that the larger birds of the larger variety were relatively fatter. Our result differs from Lee's in that the slope is 0.74 or less, never 1.0 (*i.e.*, never linear).

There is a considerable body of data on metabolism of dogs, and it seems interesting to see how metabolism varies with body size. Are the slopes nearer 1.0 (Lee) or $\frac{2}{3}$ (surface law)? We plotted in Fig. 13.12 several well-known sets of data[49], giving a slope not of 1.0, but 0.61 for Rubner's data, and 0.57 for Lusk's and Kunde's data. In no case did the slope approach unity.

Finally, Fig. 13.13 brings together on a logarithmic grid the data from Figs. 13.7, 13.10, and 13.12; it shows, by the curved line, the result of "forcing" a linear equation (by the method of least squares) on the data in Table 13.1.

We thus conclude that the basal energy metabolism of mature animals of different species tends to vary with approximately the 0.7 power of body weight and suggest that $\mathrm{Kg}^{0.7}$ be taken as reference base for comparative basal metabolism measurements.

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[42] Kleiber, M., *Hilgardia*, **6**, 315 (1932).

[43] Brody and Procter, Univ. Missouri Agr. Exp. Sta. Res. Bull. 166, pp. 89–101, 1932.

[44] Brody, Procter and Ashworth, Id. Res. Bull., 220 1934.

[45] Report of the Conference on Energy Metabolism of the Committee on Animal Nutrition, National Research Council, p. 7, 1935.

[46] Benedict[9], Table 13.1[9].

[47] Lee, R. C., "Size and basal metabolism of the adult rabbit," *J. Nut.*, **18**, 489 (1939).

[48] Grateful acknowledgments are made to C. F. Winchester and H. H. Kibler for assistance.

[49] Rubner, M., *Z. Biol.*, **19**, 535 (1883). Lusk, G., and Du Bois, E. F., *J. Physiol.*, **59**, 213 (1924). Kunde, M. M. and Steinhaus, A. H., *Am. J. Physiol.*, **78**, 127 (1926).

13.6: Relation of endogenous nitrogen, creatinine, and neutral sulfur excretion to body weight in mature animals of different species. The 0.7 power of body weight is not only a good reference base for basal *energy* metabolism but also for basal *protein* metabolism, or endogenous nitrogen and neutral sulfur excretion.[50] This is demonstrated in Figs. 13.14, 13.15, and 13.16, plotted from data in Tables 13.4 a and b and 13.6. The value of the exponent is seen to range from 0.72 (Fig. 13.14) to 0.74 (Fig. 13.16).

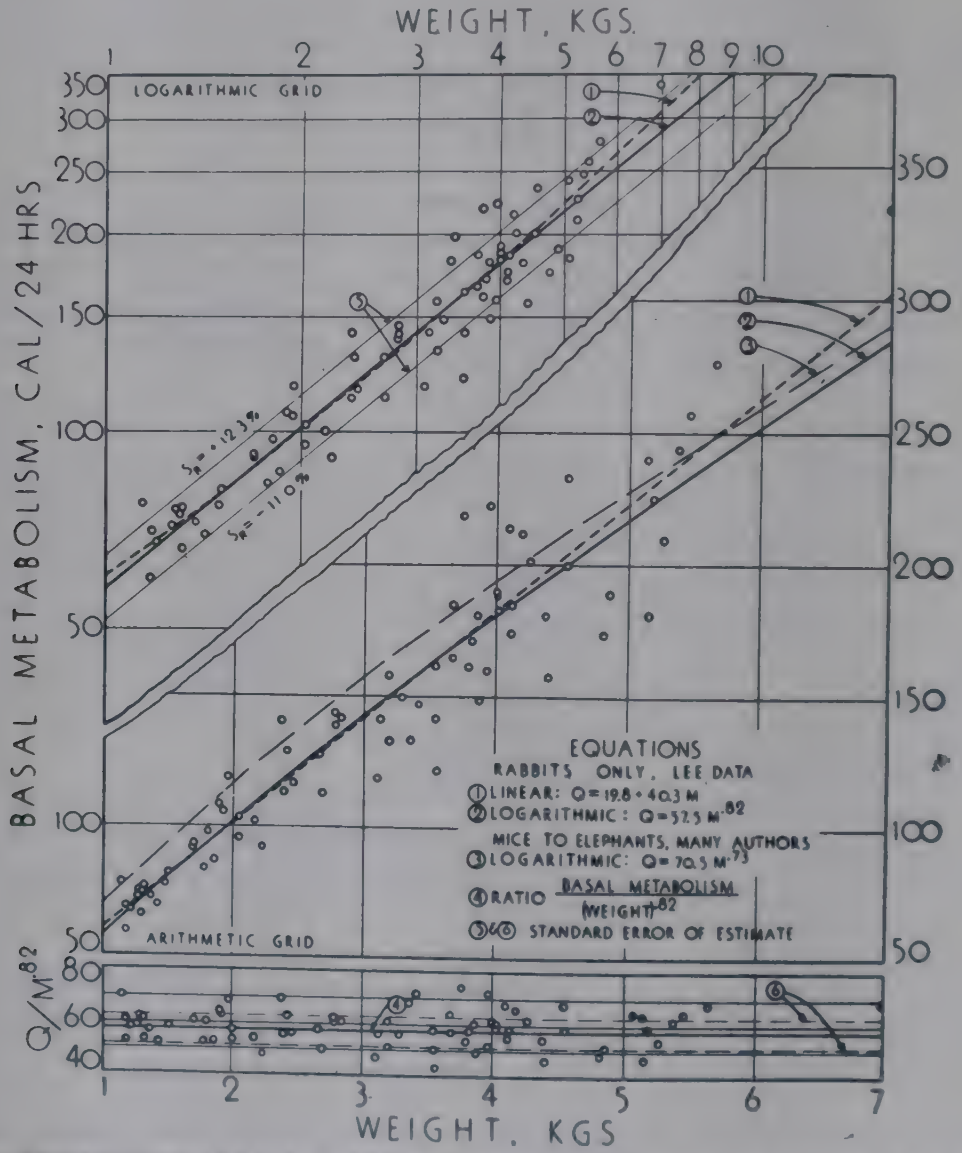

Fig. 13.10—Metabolism of Lee's rabbits plotted on logarithmic (upper left) and arithmetic (lower right) paper compared with the mice-to-elephant curve from Fig. 13.7.

The creatinine excretion, however, varies not with the 0.7 power but more directly with weight. This is shown in Fig. 13.17, plotted from Table 13.5. In other words, creatinine cannot be taken as an index of basal energy metab-

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[50] Brody, S., Procter, R. C., and Ashworth, U. S., "Basal metabolism, endogenous nitrogen, creatinine, and neutral sulfur excretions as function of body weight," Mo. Agr. Exp. Sta. Res. Bull. 220, 1934.

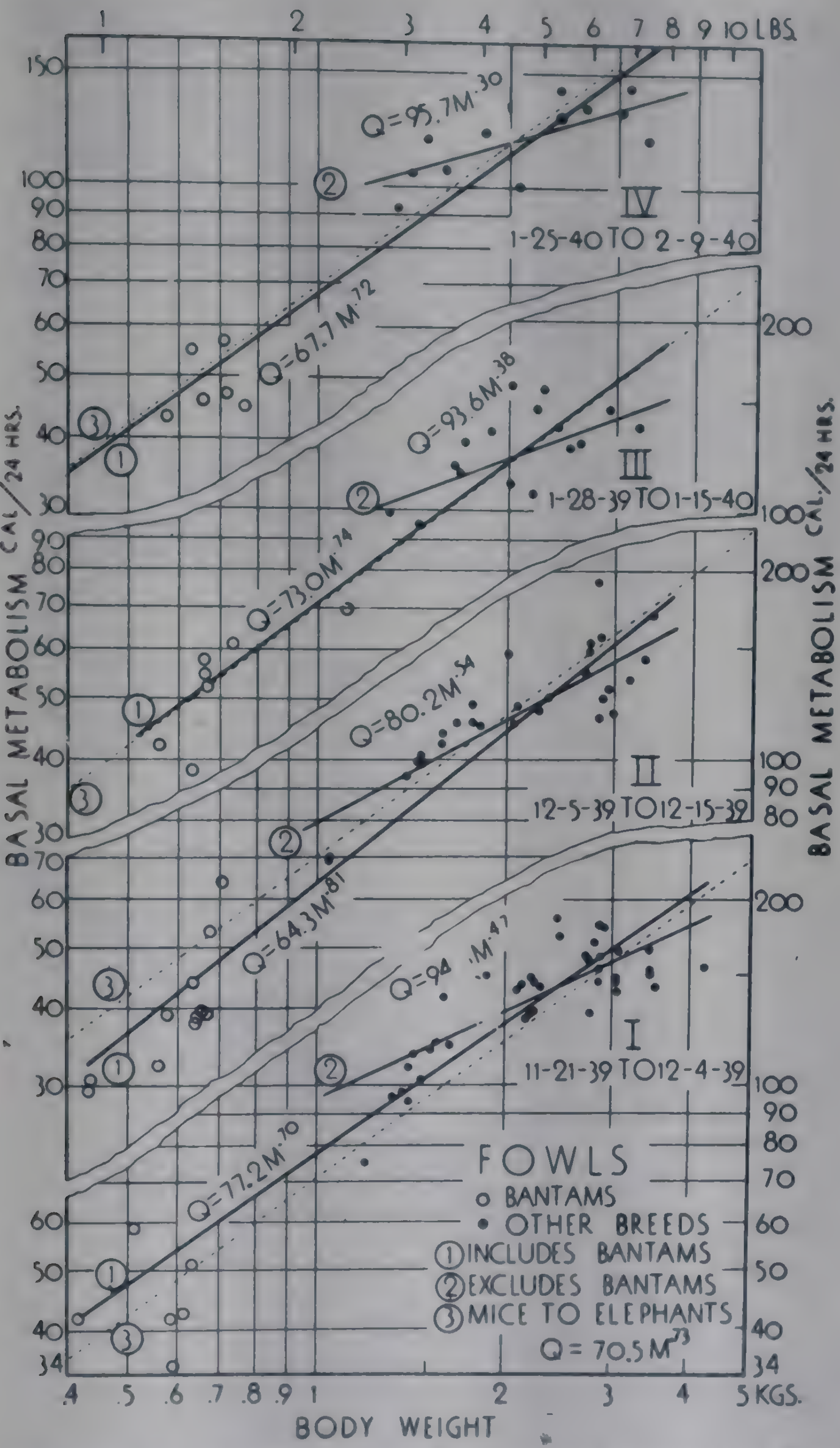

Fig. 13.11—Metabolism of two varieties (bantam and normal) of Rhode Island Red fowls compared with the mice-to-elephant equation of 13.7. The curves of the two virtually coincide, the slope being nearly 0.73. If, however, the bantams are omitted, the slope is very low.

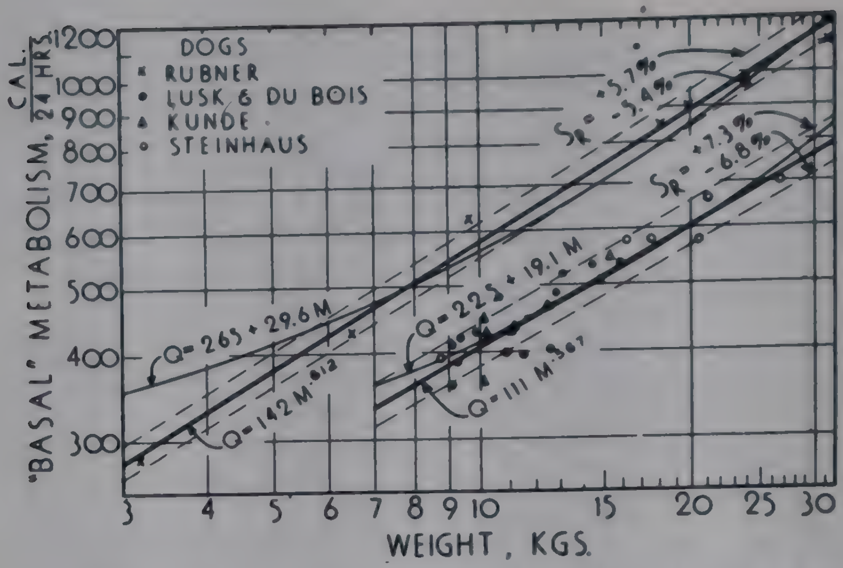

Fig. 13.12—Metabolism of three groups of dogs indicating a slope of 0.6.

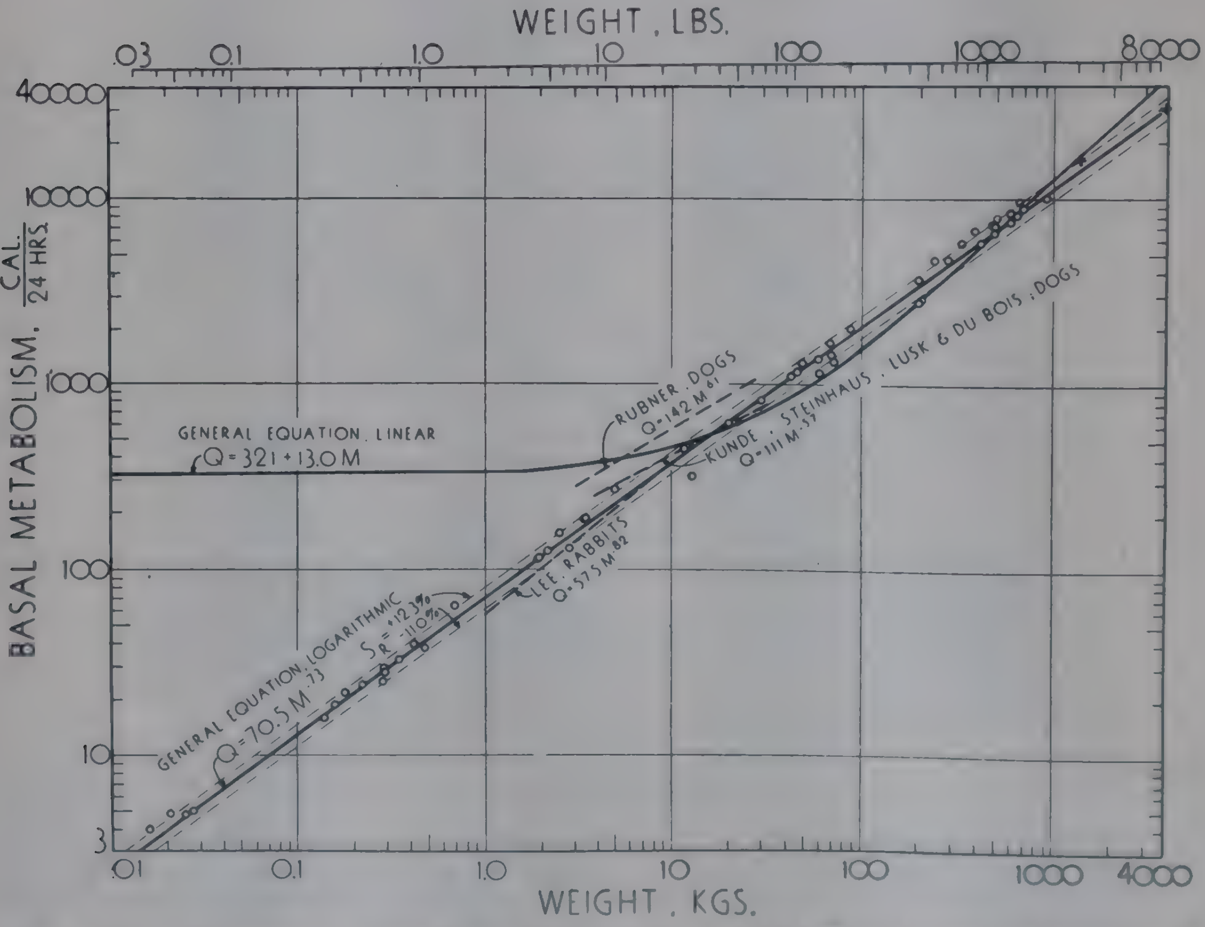

Fig. 13.13—The curves from Figs. 13.7, 13.10, and 13.12 are brought together on a logarithmic grid. Also a linear equation is shown when arbitrarily "forced" on the data by the method of least squares.

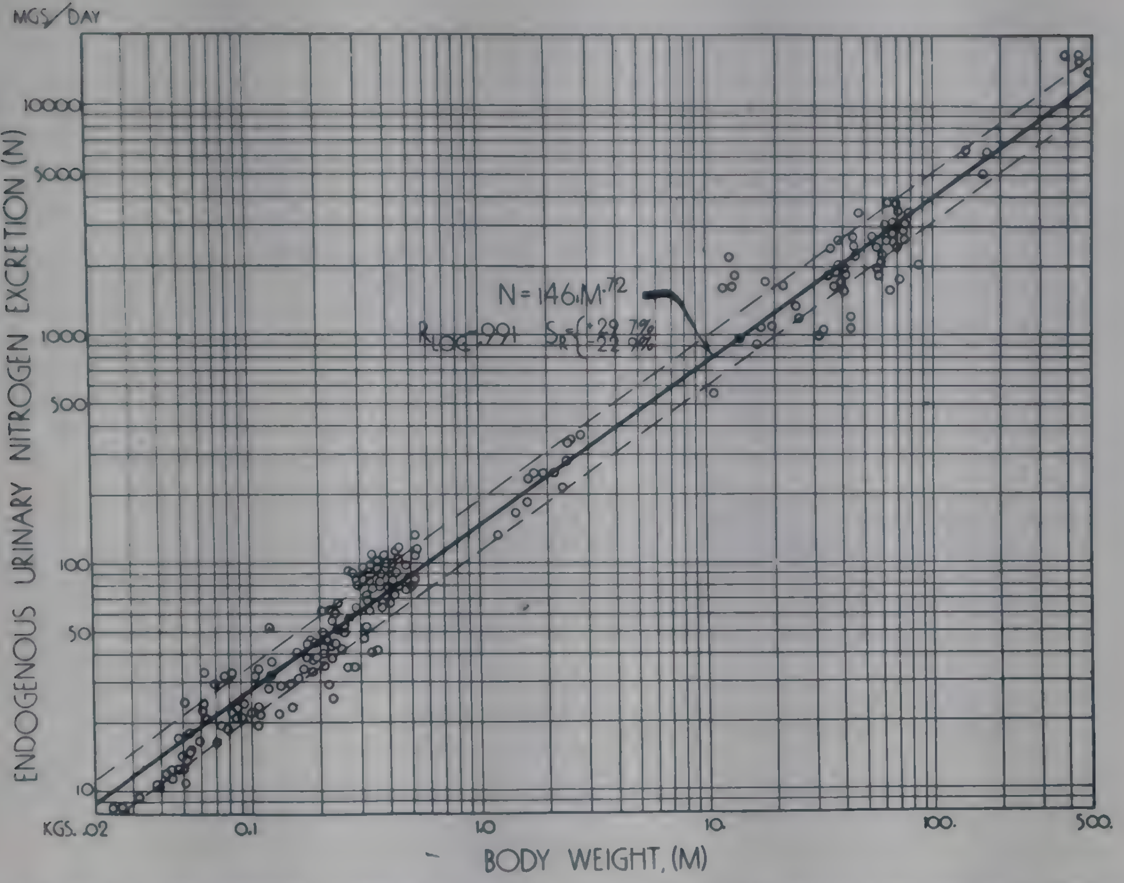

Fig. 13.14—Endogenous urinary nitrogen metabolism of mature animals of different species as function of body weight, plotted from Table 13.4b.

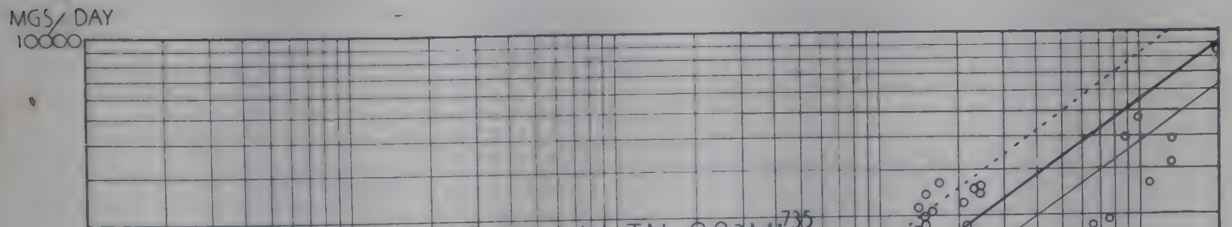

Fig. 13.15—A comparison of endogenous urinary (U.N.) and total nitrogen (T.N.) (including fecal) excretion as function of body weight plotted from Table 13.4a.

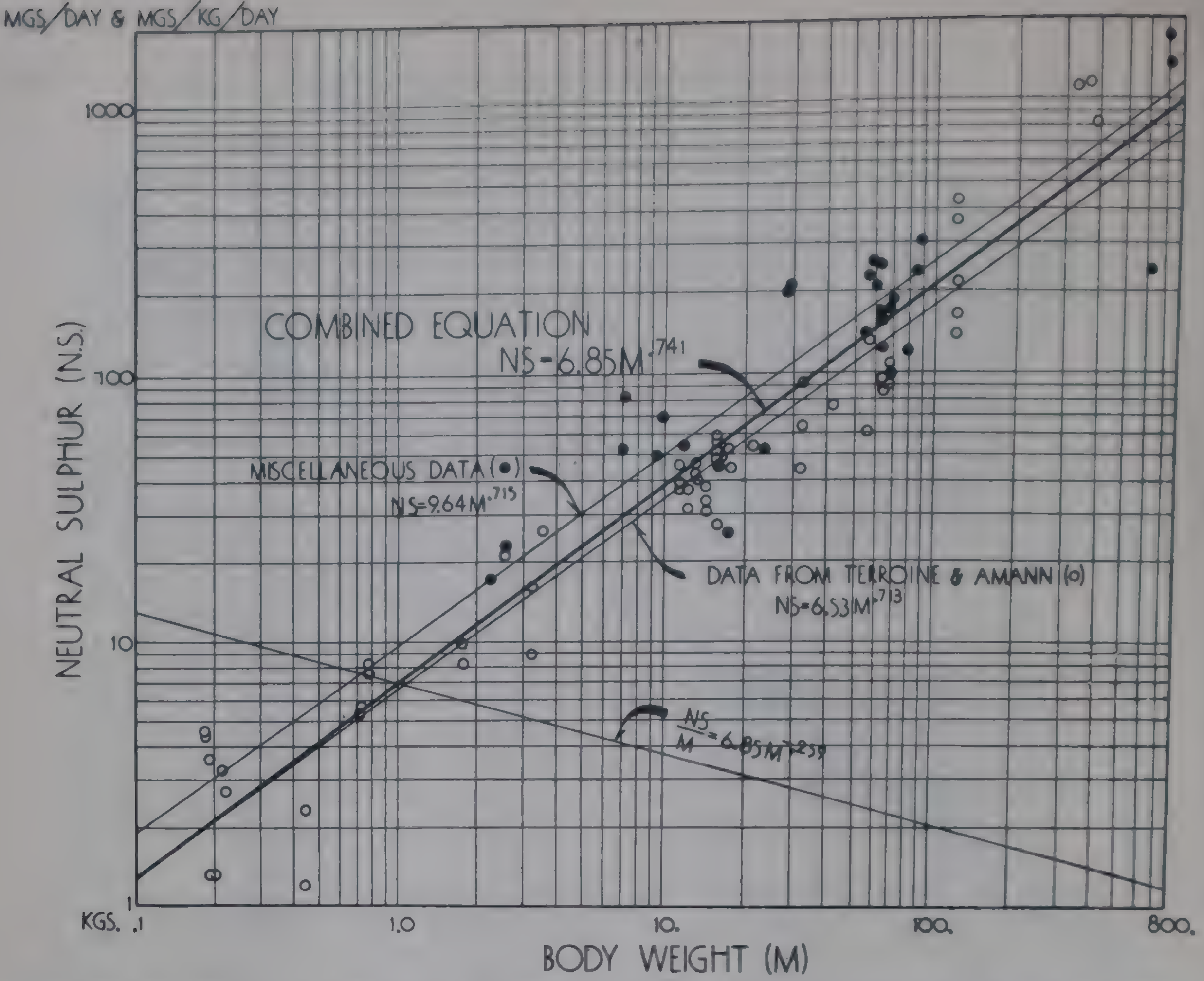

Fig. 13.16—Neutral sulfur as function of body weight, plotted from Table 13.6.

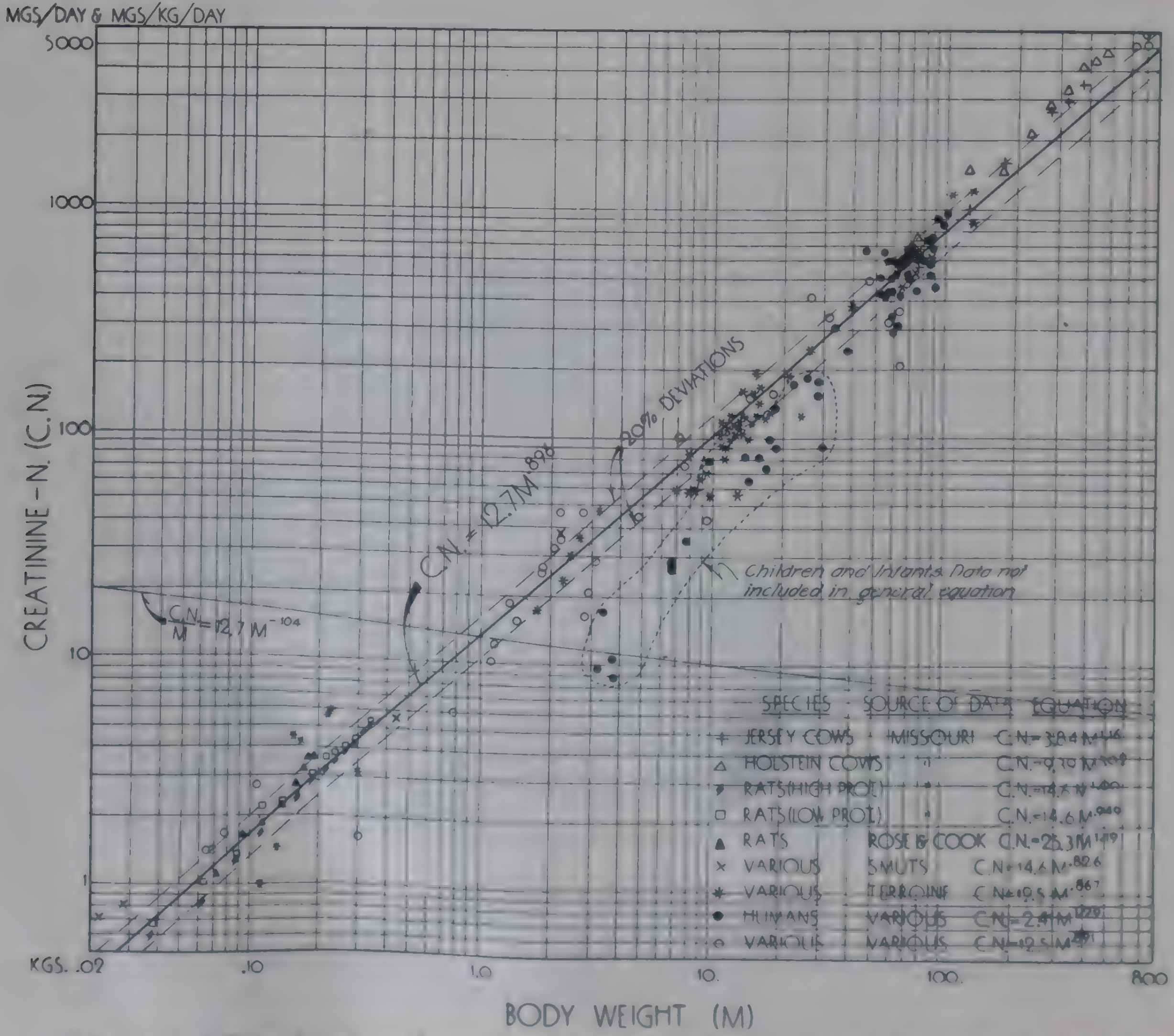

Fig. 13.17—Creatinine as function of body weight, plotted from Table 13.5.

olism, as was suggested by Palmer, Means, and Gamble.[51] These authors reported that eight men produced on the average 0.98 Cal per mg creatinine, and that nine women produced on the average 1.26 Cal per mg. We have shown[52] that the course of creatinine excretion in growing dairy cattle does not parallel that of heat production. At a body weight of 40 kg, four Cal were produced per mg creatinine; at a body weight of 400 kg, only one Cal was produced per mg creatinine.

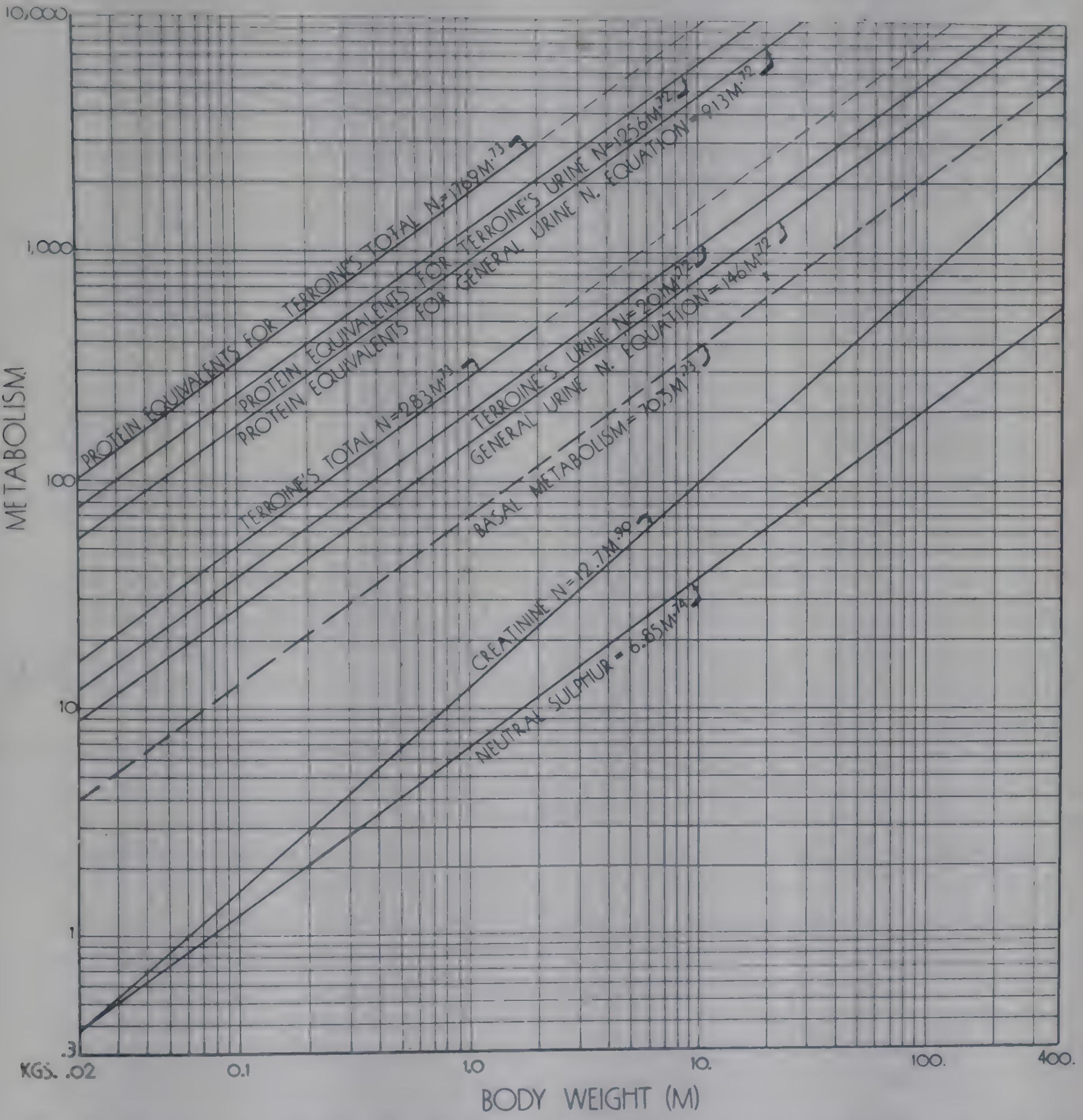

Fig. 13.18—Prediction curves for energy and protein catabolism as functions of body weight, plotted from Table 13.7.

The parallelism between basal energy metabolism, endogenous nitrogen excretion, and neutral sulfur excretion—but not creatinine excretion—is illustrated graphically in Fig. 13.18, and in the prediction Table 13.7. Such parallelism means that the ratio of endogenous urinary or total nitrogen to basal energy metabolism tends to be the same in small and large animals, namely, about 2 mg nitrogen per Cal. Practically, this means that the nutritive ratio, or the ratio of energy to nitrogen in a maintenance ration, is independent of body weight.

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[51] Palmer, W. W., Means, J. H., and Gamble, J. L., "Basal metabolism and creatinine elimination," *J. Biol. Chem.*, **19**, 239 (1914).

[52] Mo. Agr. Exp. Sta. Res. Bull. 143, pp. 58-61, 1930.

Historical and explanatory notes: In 1928 Terroine and Sorg-Matter[53] reported data on the ratio of total endogenous nitrogen excretion, *including fecal*, to basal energy metabolism in mature animals of different species, mice, rats, pigeons, chickens, and rabbits, and found it to be approximately constant, namely 2.3 to 2.9 mg N per Cal, as indicated by the following table:

Animal	Mg total endog. N per kg-hr	Cal basal metabolism per kg-hr	Mg N per Cal
Mouse	34.8	12.0	2.90
Rat	18.8	7.8	2.41
Pigeon	18.8	6.5	2.89
Chicken	10.6	4.6	2.30
Rabbit	9.0	3.4	2.65
Dog	6.7	2.4	2.80
Man	2.2	0.933	2.32

They also reported that changes in external temperature have the same relative influence on total endogenous nitrogen excretion as on basal metabolism; that the ratio of total endogenous nitrogen to basal energy metabolism remains constant, regardless of temperature; and that, therefore, the minimum nitrogen excretion, like the minimum energy metabolism, is attained only at thermal neutrality.

In 1935 Smuts[54] reported similar data (Table 13.4b), but on endogenous urinary nitrogen alone (not including fecal N), and the energy metabolism was measured on the *same* animals (which Terroine did not do). The conditions were strictly basal. The range in live weight of Smuts' animals is much wider (from 20-g mice to 79-kg pigs) than the range of Terroine's animals (from 15-g mice to 1.6-kg chickens).

Smuts' results confirmed Terroine and Sorg-Matter that the ratio of endogenous nitrogen to basal metabolism is remarkably constant for animals of different live weight, as indicated by the following ratios of mg urinary nitrogen to Calories basal metabolism: mice, 1.92; rats, 2.00; rabbits, 2.04; pigs, 2.10; average of all measurements, 1.99. If one recalls that Terroine reported the ratios in terms of total (including fecal) nitrogen to Calories, while Smuts reported his data in terms of urinary nitrogen to Calories, the differences between the N/Cal ratios of these two investigators probably disappear.

Incidentally, Bonnet[55] found that the N/Cal ratios of poikilotherms, namely frogs and tortoises, remain constant at different environmental temperatures, ranging from 2° to 30°; they rise and fall together at a constant ratio with temperature changes. In the frog the average of this ratio was 7.2; but in the tortoises it was 2.8, very near the average found by Terroine and Sorg-Matter for homeotherms. Within each of these species, however, this ratio remained constant for different environmental temperatures. Bonnet suggests that reptiles are "biochemically intermediate" between homeotherms and poikilotherms.

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[53] Terroine, E. F., and Sorg-Matter, H., *Arch. Intern. Physiol.*, **29**, 121 (1920); **30**, 115, 126 (1928).

[54] Smuts, D. B., *J. Nut.*, **9**, 403 (1935).

[55] Bonnet, R., *Arch. Intern. Physiol.*, **37**, 105 (1933).

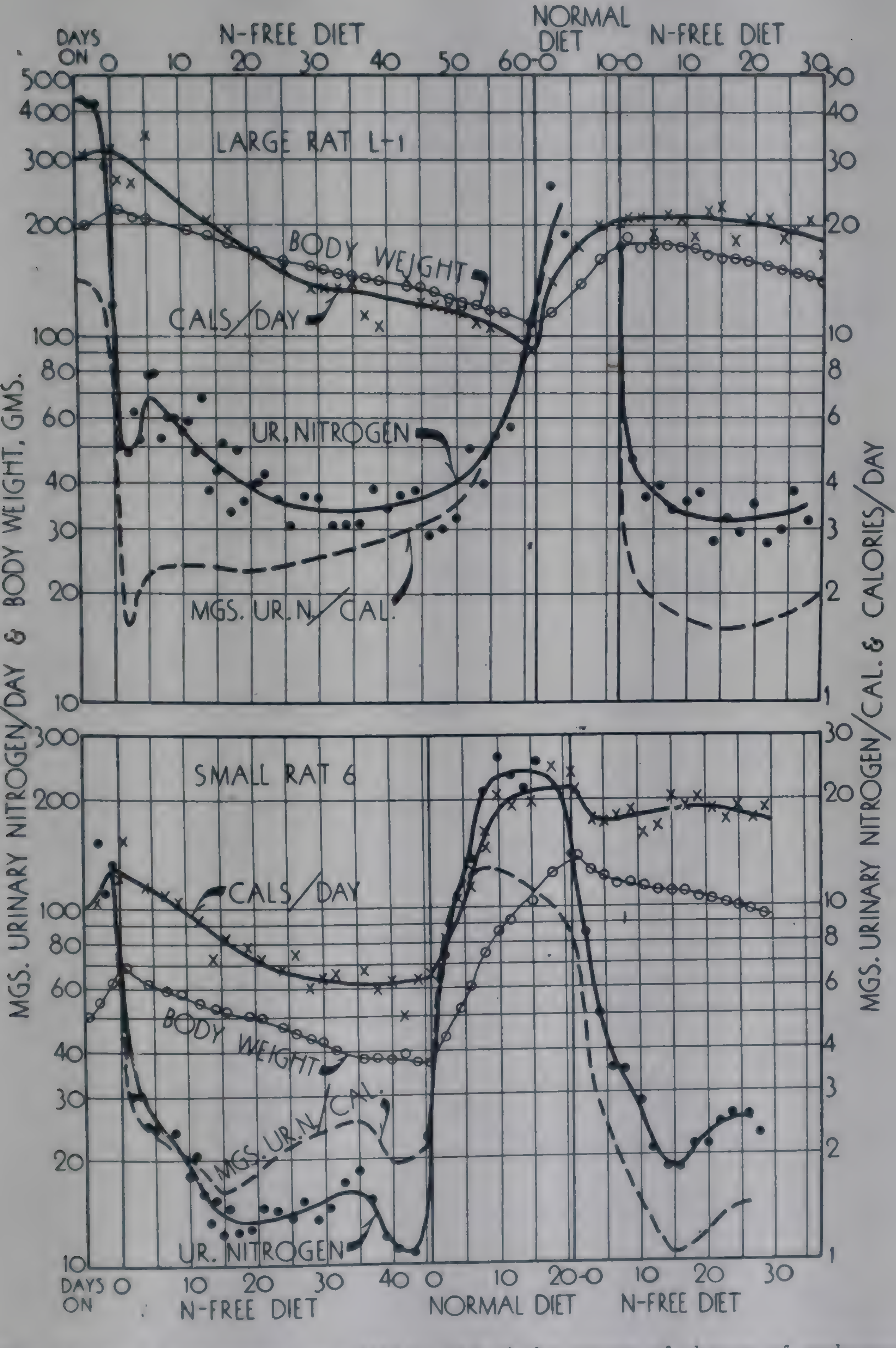

Fig. 13.19—A comparison on arithlog grid of the course of change of endogenous nitrogen with basal metabolism and with body weight with time on N-free diet (Fig. 1, p. 8, Missouri Res. Bull. 223). See page 353 for discussion.

Creatinine: Fig. 13.17, based on Table 13.5, includes data on creatinine nitrogen excretion of animals ranging in weight from 0.02 to 800 kg, thus furnishing a broad basis for generalization. Equation (13.2) was fitted to the data by the method of least squares. It appears that for the Missouri data, which represent growing animals, and for animals of different size of the *same species*, the creatinine excretion is directly proportional to body weight (the value of the exponent is near unity). For men of different weight the creatinine excretion increases even more rapidly than body weight (the exponent is 1.29). But for mature animals of *different species* the creatinine excretion increases with the 0.83 to 0.89 power of body weight. Since the endogenous nitrogen increases with but the 0.72 power of body weight, the creatinine nitrogen percentage in the endogenous urinary nitrogen increases with increasing body weight. The ratio of creatinine to total endogenous urinary N rises with increasing body weight from 4 per cent for 20-g animals to 30 per cent for 1000-kg animals. *Creatine nitrogen does not, therefore, vary directly (i.e., linearly) with either endogenous nitrogen metabolism or with basal metabolism, but more nearly with body weight.*

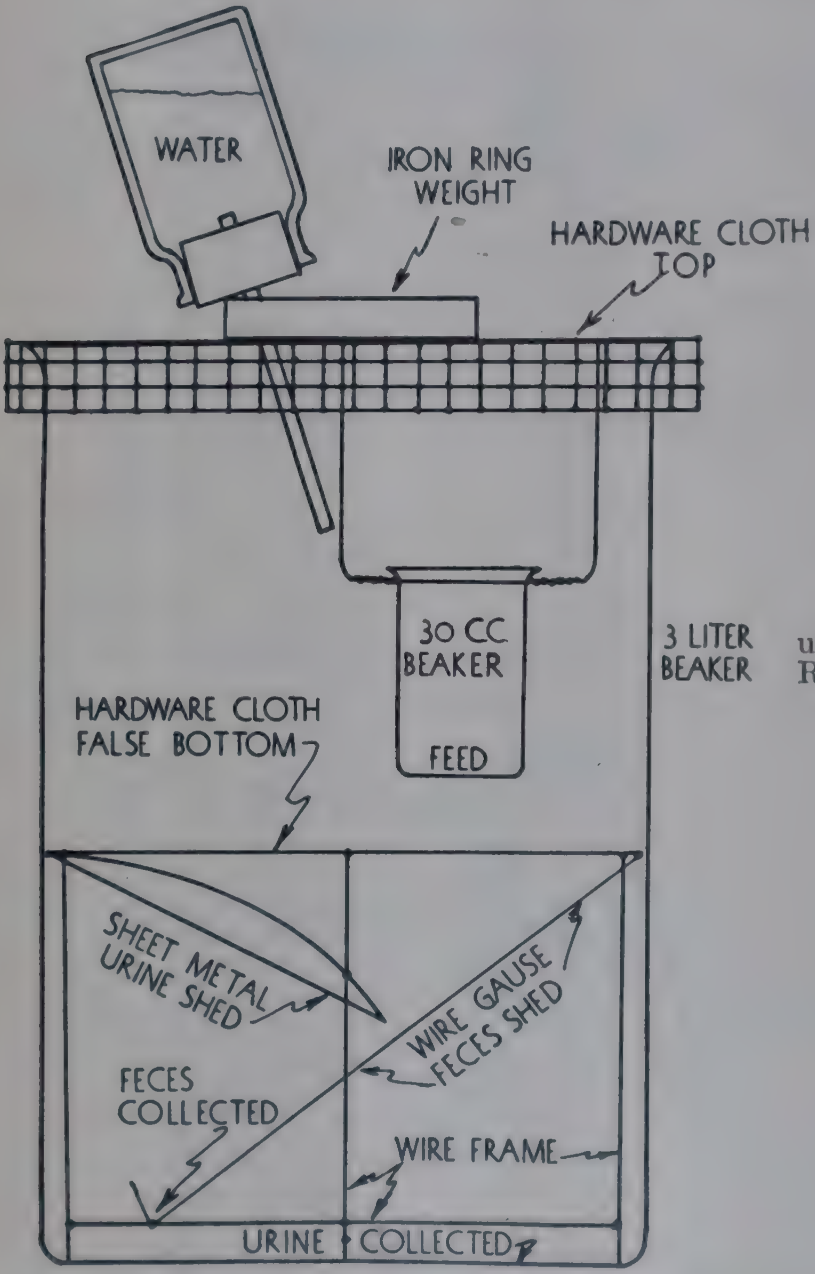

Fig. 13.20—Method of collecting urine from rats (Fig. 2, Missouri Res. Bull. 228, p. 9).

Neutral sulfur: The data points in Fig. 13.16 (plotted from Table 13.6) for neutral sulfur seem to be widely scattered, but the average slope is of the same order of magnitude as the slopes of the basal metabolism and endogenous nitrogen curves.

As regards the erratic distributions of the neutral-sulfur data, Folin[56] reported that neutral sulfur excretion tends to be independent of the protein intake. No dietary precautions would, therefore, seem to be needed. A large literature has, however, recently developed indicating that Folin's conclusion with regard to the constancy of neutral sulfur is not absolutely true. Since no special dietary precautions were taken in securing the neutral sulfur data, and since the diet is an influencing factor after all, the erratic distribution of the data becomes understandable.

According to Amann[57], the neutral sulfur excretion is the same on low as on "normal" protein diets, but it is increased on high-protein diets. When the dietary protein is increased 15 times, the neutral sulfur excretion is tripled. The amount of neutral sulfur is thus not strictly endogenous; it is not altogether independent of the diet, although it is constant in comparison with total sulfur excretion. According to Amann, the factors affecting the metabolism of energy also affect the excretion of neutral sulfur; but the neutral sulfur excretion is not definitely proportional to calorie production, as is the case with endogenous nitrogen.

13.7: Summary. Basal energy metabolism does *not* vary directly with simple body weight, $W^{1.0}$; with $W^{\frac{2}{3}}$, which would be proportional to surface area if different animals were geometrically and physically similar, which they are not; nor with anatomic surface area, which is not a constant for a given living animal. Basal metabolism varies directly with what we called, for lack of a more direct designation, *metabolically effective body weight*, defined by W^b. The W represents body weight (we also used interchangeably the symbols M and X); b represents the slope of the curve when plotted on logarithmically coordinate paper, and is easily computed from the given data. By this method we found that the value of b is 0.73 for the data in Table 13.1, including animals ranging in weight from mice to cattle, and perhaps elephants.

Interestingly enough, the value of b also turned out to be 0.73 for Benedict's monumental data given in Table 13.2, provided that several evidently atypical data are omitted. If these atypical data are not omitted, the value of b for Benedict's data is 0.76.

On the other hand, the value of b for dogs of different size is only 0.6; for mature birds of different species the value of b ranges for several sets of data from 0.62 to 0.70. For mature Rhode Island Red fowls of two varieties, it was 0.73 if both varieties were included, and only 0.5 if the bantam variety was excluded. For mature rabbits of different size, as reported by Lee, the value of b was 0.82. It is particularly variable for man, depending on the age range, although we suggest different constants for the DuBois linear formula (Fig. 13.6). We are not, however, concerned with human data, which are taken care of by DuBois formula. While we employ the reference base $W^{0.73}$ throughout this book, yet because of these variations, we are inclined to drop the second decimal (which gives the impression of greater constancy or precision than is justified by the variability of the data) and suggest that $W^{0.7}$ be adopted for the reference base for basal metabolism; that increasing body weight 100 per cent tends to be most nearly associated with a differential metabolic increase not of 100 per cent but only of 70 per cent.

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[56] Folin, O., *Am. J. Physiol.*, **13**, 116 (1905).

[57] Amann, O. V., *Arch. Intern. Physiol.*, **37**, 121, 168 (1933); Amann, O. V., and Mourot, G., *Id.*, p. 150; Razafimahery, R., *Ann. Physiol.*, **11**, 261, 322 (1935); Terroine, E. F., *Id.*, p. 354. See also Lewis, H. B., "The relative eliminations of sulfur and nitrogen in the dog in inanition and subsequent feeding," *J. Biol. Chem.*, **26**, 61 (1916); Carpenter, T. M., "Composition of urine of steers as affected by fastings," *Am. J. Physiol.*, **31**, 519 (1927); Wilson, H. E. C., "Relation between sulfur and nitrogen metabolism," *Biochem. J.*, **19**, 322 (1925); **20**, 76 (1926); *J. Physiol.*, **77**, 240 (1933); Morgulis, S., Bollman, V. L., and Brown, H. I., "Urinary sulfur partition in fasting dogs," *J. Biol. Chem.*, **77**, 627 (1928).

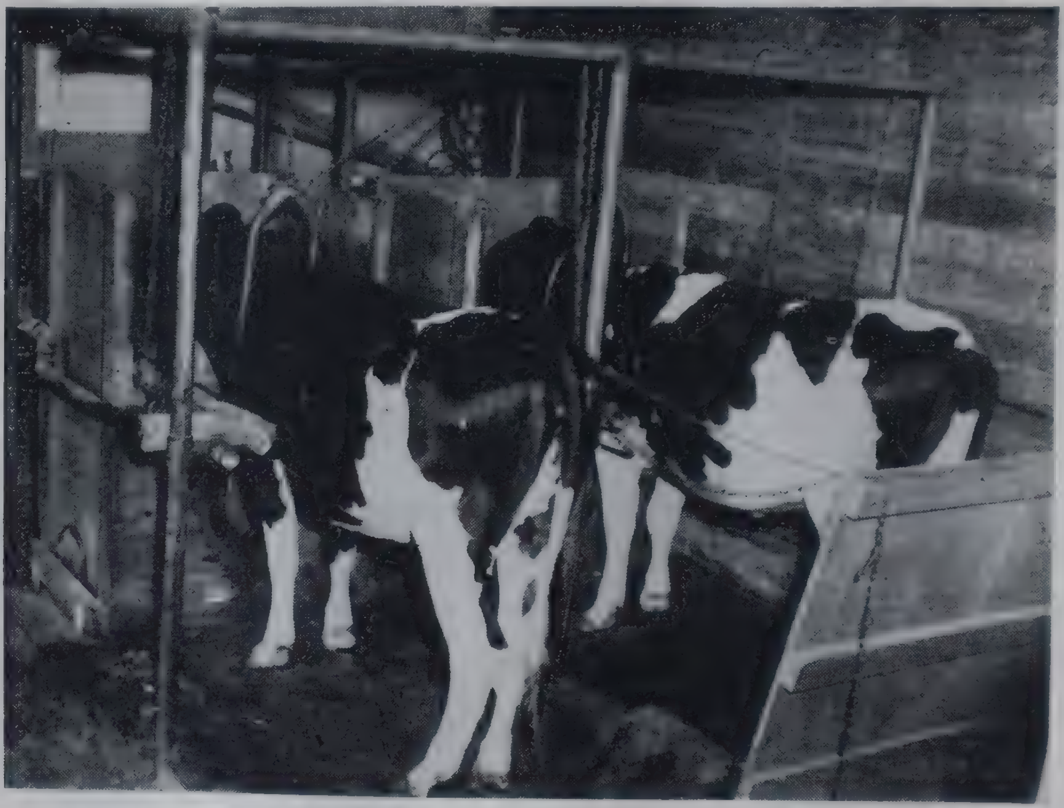

Fig. 13.21a—Method of collecting cow's urine and feces into separate containers as used in our laboratory. The motor and gear assembly keep the belts turning continuously toward the center. Feces which fall on the belts are carried through the trapdoors and scraped off into the tubs. Urine flows down the inclined belts and is directed by the funnel-shaped pans into the bottles. This apparatus was patterned after the installation by Ritzman and Benedict, N. H. Agr. Exp. Sta. Bull. 240.

This reference base $W^{0.7}$ has broader implications than appear, because it is also the reference base for many other processes. Thus the endogenous urinary nitrogen and sulfur excretion also vary with $W^{0.7}$. Creatinine, however, though a component of the endogenous nitrogen, reflects more nearly the mass of the supporting muscles than that of the vital visceral organs and so varies more nearly with $W^{1.0}$ than with $W^{0.7}$.

Special attention is given to the "surface law", the best formulation of which was made over a century ago but which is frequently re-discovered by

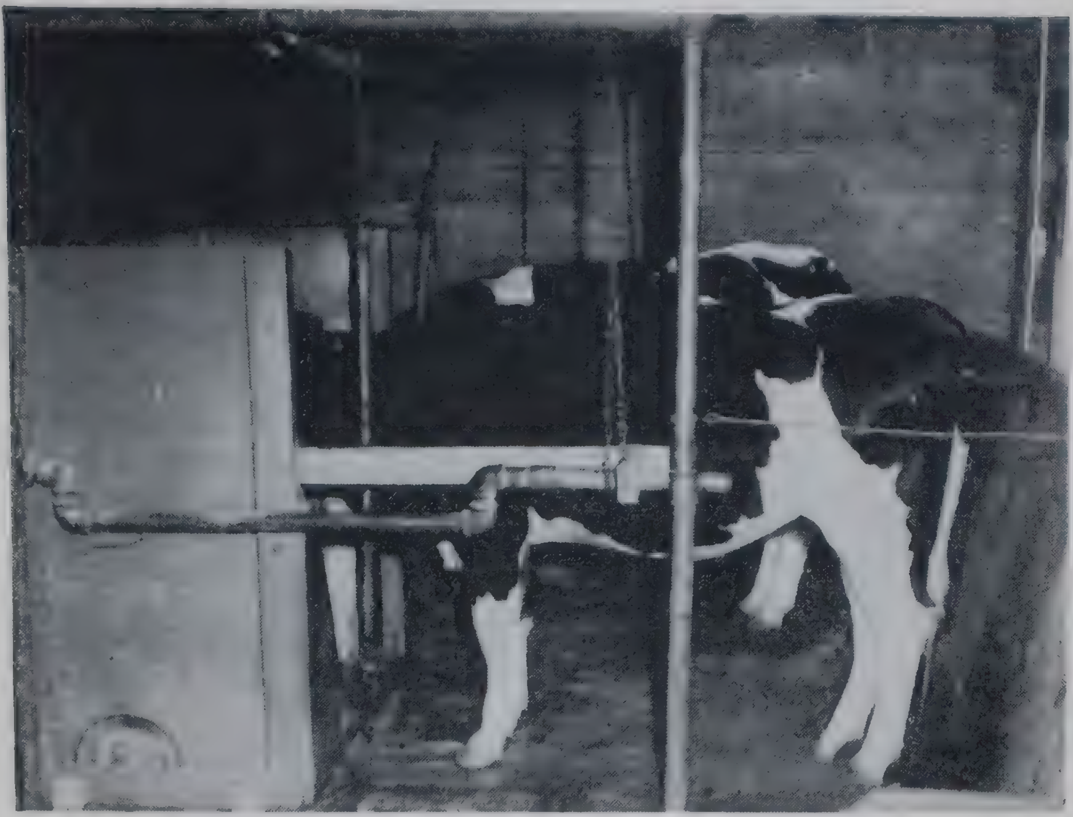

Fig. 13.21b—See caption of 13.21a.

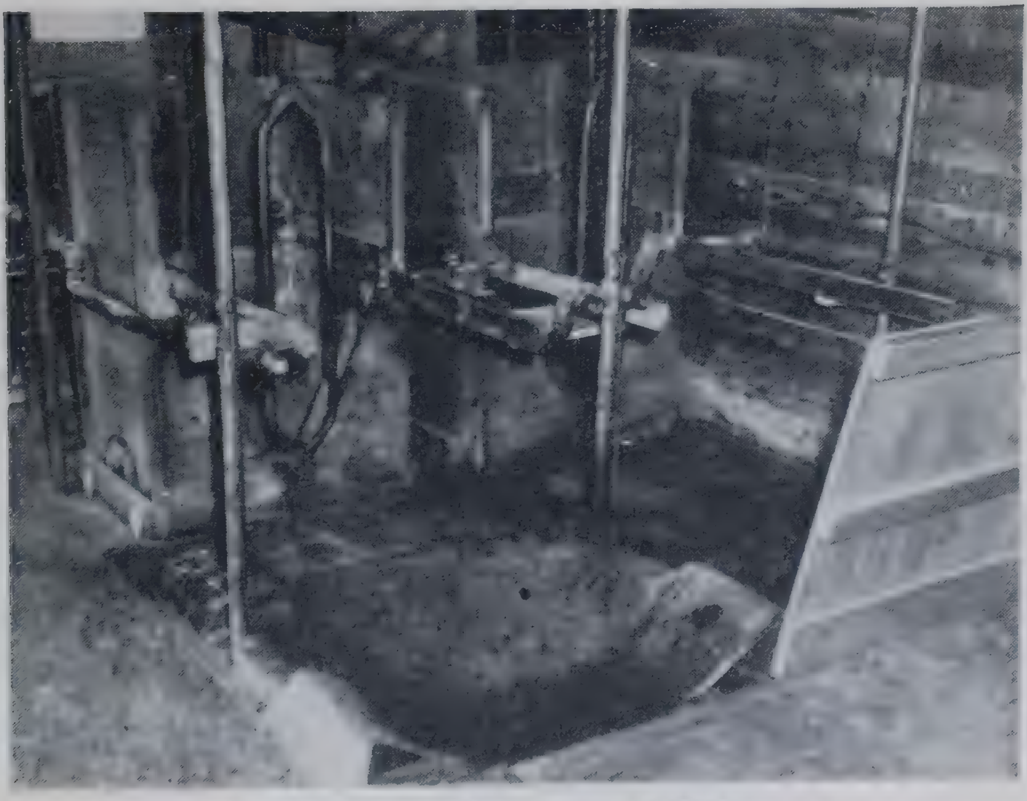

Fig. 13.21c—See caption of 13.21a.

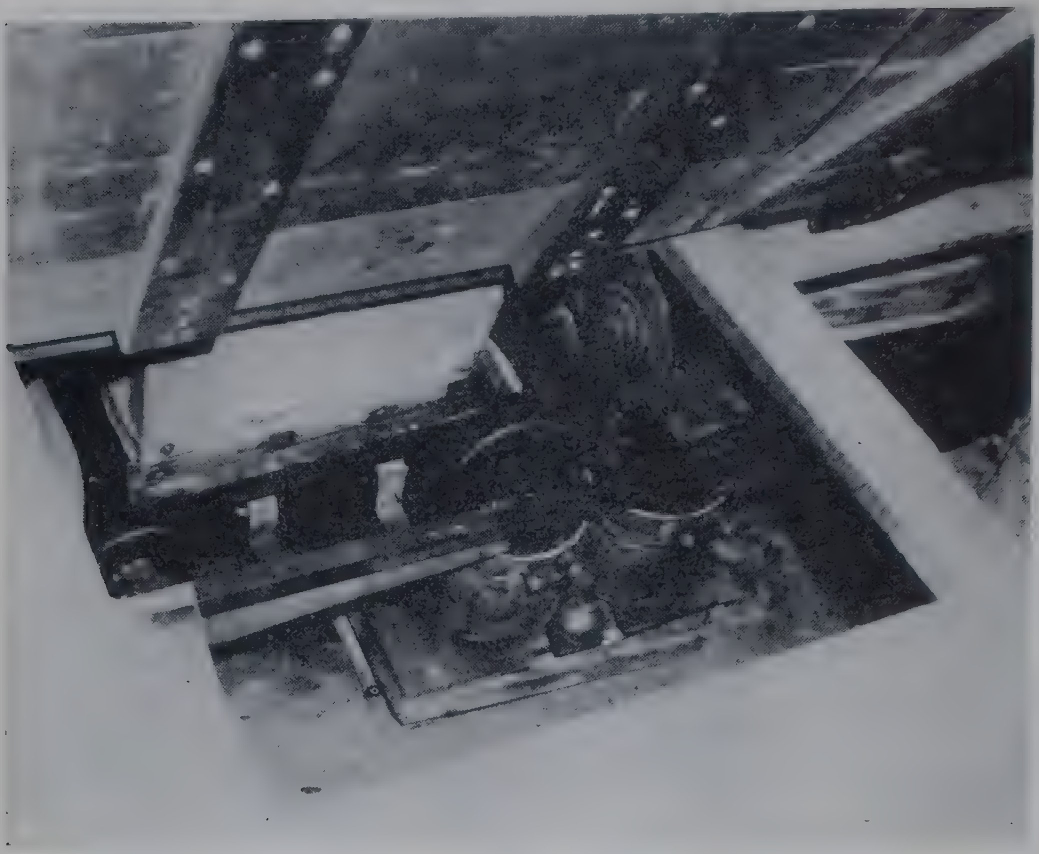

Fig. 13.21d—See caption of 13.21a.

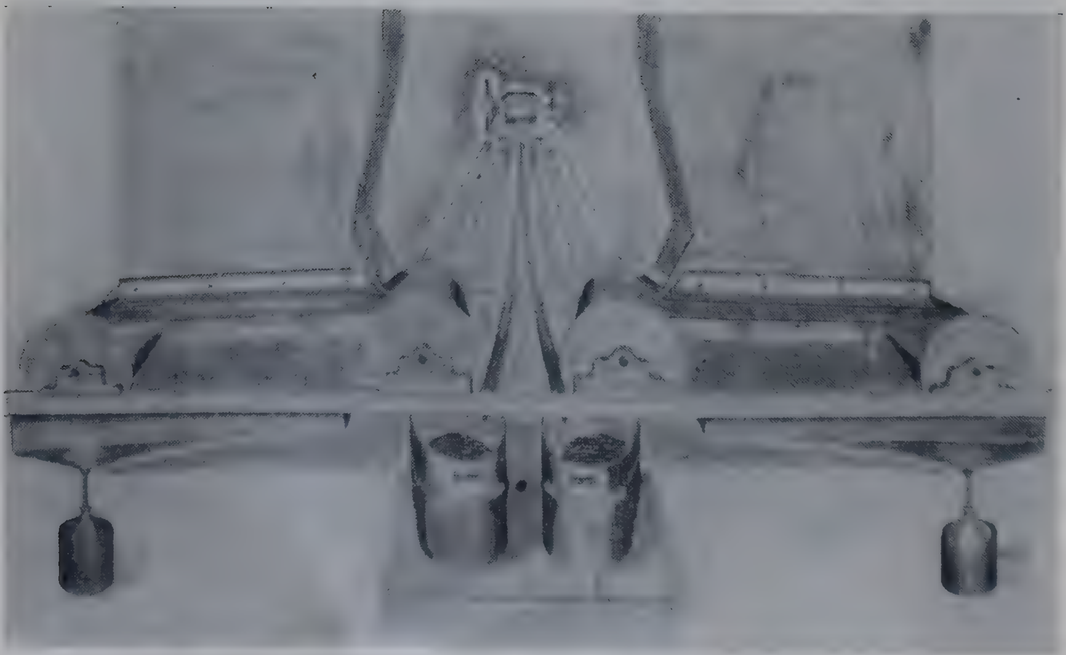

Fig. 13.21e—See caption of 13.21a.

numerous investigators. This is typical of much scientific work, and of life in general: continuous forgetting and re-discovering of old truths.

The "surface law" is reasonable enough except that anatomic surface cannot be measured with precision; that physiologic, or "free", or "metabolically effective", surface is not identical with anatomic surface; that external surface is not the direct "cause" of a given metabolic level, although the correlation of metabolic level with surface area may have been an evolutionary prerequisite for survival—an evolutionary, or "remote cause".

The direct control of the metabolic level resides not in the external surface but in the neuro-endocrine system which, for geometric and mechanical "reasons" discussed in the text, tends to vary in size with surface area rather than with simple body weight. So it comes about that the size of the neuro-endocrine components, the surfaces, the heat dissipation, and the heat production all tend to vary in parallel (Ch. 17). They may all be said to vary with W^b, and the value of b tends to be near 0.7. It will be shown presently that the quantity of milk-energy production (Chs. 21, 22) and of egg-energy production (Ch. 23) likewise tends to vary with $W^{0.7}$, as does basal energy metabolism and endogenous protein metabolism. This brings out the broad significance of the proposed reference base $W^{0.7}$, which may be termed "physiological" weight in contrast to $W^{1.0}$, which is the "physical" or gravitational weight.[58] These interrelations and the importance of W^b will be further discussed in Chapters 14, 15, 17, 21, 22, 23, and 24. In the meantime it is suggested that $W^{0.7}$ be tentatively adopted as reference base for basal-energy metabolism, endogenous nitrogen excretion, milk-energy production, egg-energy production and related processes.

The following tables are self-explanatory summaries and "predictions".

[58] Brody, S., "Relativity of physiologic time and physiologic weight," *Growth* **1**, 60 (1937).

TABLE 13.1. Data on Basal Metabolism.

Animal and Sex	No. of Trials or Animals	Body Weight		Basal Metabolism Cal/Day	% Deviation of Computed From Observed	Sources of Data
		Kgs.	Lbs.			
Elephant, 1 male & 1 female	3	3833	8450	30924**	+2	Missouri (unpublished)
Elephant, male	1	1360	2998	16020**	+1	Missouri (unpublished)
Beef steer, Hereford, 815	10	922	2033	9996	−6	Missouri (unpublished)
Beef steers, Hereford	E	700	1543	8910	+3	Missouri Res. Bulls. 166 & 176 (1932)
Horses, Percheron females	E	675	1488	9743	+15	Missouri Res. Bulls. 166 & 176 (1932)
Horses, Percheron geldings	E	650	1433	8188	−0.3	Missouri Res. Bulls. 166 & 176 (1932)
Beef steers, grade shorthorn	2	615	1356	8554*	+8	Mitchell *et al*, J. Agric. Res. **45**, 163 (1932)
Beef steers (C & D)	16	601	1325	7420*	−4	Benedict & Ritzman, Publ. 377, Carnegie Inst. Wash. (1927)
Dairy cow, Holstein, 604	4	508	1120	7958	+16	Missouri (unpublished)
Dairy cows, Holstein	E	500	1102	7210	+6	Missouri Res. Bulls. 166 & 176 (1932)
Beef cows, Hereford	E	500	1102	6600	−3	Missouri Res. Bulls. 166 & 176 (1932)
Dairy bulls, Jersey	E	500	1102	7307	+8	Missouri Res. Bulls. 166 & 176 (1932)
Dairy cows, Jersey	E	420	926	5865	−2	Missouri Res. Bulls. 166 & 176 (1932)
Horse	3	392	864	6923*	+22	Zuntz & Hagemann, Landw. Jahrb. 27 Ergeb.-Bd. III (1898)
Beef Steers, shorthorn	5	336	741	5781*	+14	Forbes, Kriss, *et al.*, J. Agric. Res., **48**, 1003 (1931)
Horses, Shetland ponies, 1 gelding 1 female	44	281	619	4683*	+6	Missouri (unpublished)
Beef Steers (E. & F.)	2	244	538	4725*	+18	Benedict & Ritzman (see above)
Swine, Duroc Jersey males	E	200	441	3660	+6	Missouri Res. Bulls. 166 & 176 (1932)
Swine, Duroc Jersey females	E	200	441	2780	−20	Missouri Res. Bulls. 166 & 176 (1932)
Pigs, 1 Middle White & 1 Berkshire	E	200	441	2760	−20	Deighton, J. Agric. Res., **19**, 140 (1929)
Pigs, males & females	5	72	159	1342	−18	Smuts, Ill. Ph. Dissertation (1933), Urbana, Illinois
Horses, Shetland pony gelding	3	88	194	2028*	+7	Missouri (unpublished)
Human, Am. white males	E	70	154	1700	+6	Benedict, *et al;* & Boothby & Sandiford } See Mo. Res. Bull. 166
Human, Am. white females	E	60	132	1370	−4	Benedict, *et al;* & Boothby & Sandiford
Sheep, ewes	3	42.7	94	1105	−0.6	Benedict & Ritzman, Wiss. Arch. Landw. Abt. B., **1**, 1 (1931); N. H. Agric. Expt. Sta. Tech. Bulls. 43 & 45 (1930)
Sheep, rams	3	49.5	109	1306	+5	Benedict & Ritzman (see above)
Sheep, Dorset wethers	E	70	154	1440	−10	Missouri Res. Bull. 166–176 (1932)
Sheep, Dorset ewes	E	60	132	1135	−21	Missouri Res. Bull. 166–176 (1932)
Sheep, Australian merino ewes	16	46.5	103	1168*	−1	Lines & Pierce, Bull. 55 Council for Sc. & Ind. Res. Comm. Australia, Melbourne
Dogs, male and female	E	30.66	66.1	807	−7	Various (p. 84 Mo. Res. Bull. 166)
Dogs, male and female	E	5.0	11.0	266	+16	Various (p. 85 Mo. Res. Bull. 166)
Dogs, male	5	20.4	45.0	618	−4	Steinhaus } See Kunde, Am. J. Physiol., **78**, 127 (1926) **& 80**, 681 (1927)
Dogs, male and female	13	13.1	28.9	319	−32	Boothby
Dogs, female	14	11.7	25.8	446	+4	Lusk
Dogs, male and female	7	11.5	25.3	446	+5	Kunde
Rabbits, male and female	E	3.5	7.72	189	+7	Various (p. 85 Mo. Res. Bull. 166)
Domestic fowls, male & female	E	3.5	7.72	187	+6	Mitchell, Card, Haines, J. Agric. Res., **34**, 349 (1927)
Goose, female	5	3.31	7.30	204	+19	Hari, Biochem. Z. **78**, 313 (1917)
Domestic fowls, R. I. R. (day expts)	8	2.57	5.66	157	+11	Benedict, Landauer & Fox, Storrs Agr. Exp. Sta. Bull. 177 (1932)
Fowls, R. I. R. Hens (day expts)	3	2.00	4.41	112	−4	Benedict, Landauer & Fox (see above)
Fowls, R. I. R. Cocks (night expts)	7	2.89	6.37	131	−15	Benedict, Landauer & Fox (see above)
Fowls, R. I. R. Hens (night expts)	10	1.99	4.39	112	−4	Benedict, Landauer & Fox (see above)

TABLE 13.1.—*Continued*

Cat	1	2.50	5.51	196	+42	Haldane, J. Physiol., **13**, 419 (1892)
Rabbits, male and female	10	2.20	4.85	123	−2	Smuts (see above)
Ducks, females	5	0.925	2.04	83.3	+25	Hari & Kriwuscha, Biochem. Z., **88**, 345 (1918)
Guinea pigs	E	0.70	1.54	63.7	+17	Various (p. 85 Mo. Res. Bull. 166)
Guinea pigs, male and female	9	0.43	0.95	39.0	+3	Smuts (see above)
Pigeon, males	E	0.34	0.75	27.2	−15	Riddle (p. 86 Mo. Res. Bull. 166)
Doves, males	E	0.15	0.33	16.1	−8	Riddle (p. 59 Mo. Res. Bull. 166)
Rat, male	1	0.797	1.757	47.0	−21	Benedict, Horst, & Mendel, J. Nutrition, **5**, 581 (1932)
Rat, male	1	0.706	1.556	51.9	−5	Benedict, Horst, & Mendel, J. Nutrition, **5**, 581 (1932)
Rat, male	1	0.723	1.593	45.5	−18	Benedict, Horst, & Mendel, J. Nutrition, **5**, 581 (1932)
Rats, males	12	0.484	1.067	37.3	−10	Benedict, Horst, & Mendel, J. Nutrition, **5**, 581 (1932)
Rats, males	12	0.351	.676	32.3	−1	Benedict, Horst, & Mendel, J. Nutrition, **5**, 581 (1932)
Rats, high-protein males	E	0.29	0.64	28.9	+1	Missouri (Res. Bull. 166 & 176)
Rats	E	0.29	0.64	28.1	−1	Benedict & MacLeod (p. 73 Mo. Res. Bulls. 166 & 176)
Rats, male and female	E	0.29	0.64	24.7	−13	Mitchell & Carman (p. 73 Mo. Res. Bulls. 166 & 176)
Rats, male and female	23	0.226	0.50	23.6	−4	Smuts (see above)
Rats, females, milk diet, summer 1934	28	0.183	0.40	21.1	+4	Missouri (unpublished)
Rats, normal females	143	0.141	0.31	15.6	−7	Hemmingsen Hemmingsen } Skand. Arch. Physiol., Vols. 67 & 68 (1933–4)
Rats, ovariectomized	151	0.160	0.35	18.4	0	
Mice, quiet male & female	224	0.0276	0.061	5.0	−1	Davis & Van Dyke, J. Biol. Chem., **100**, 455 (1933)
Mice, sleeping male & female	11	0.0276	.061	3.67	−27	
Mice, male & female	9	0.025	.055	7.84	+66	Smuts (see above)
Mice, male & female	32	0.025	.055	4.74	+0.6	Benedict & Fox, Pflugers Arch., **231**, 30 (1933) see also Davis & Van Dyke
Mice, male & female	3	0.021	.046	4.81	+16	Giaja and Males, Ann. Physiol., **4**, 875 (1928)
Mice, male & female	4	0.016	.035	3.95	+17	Aszodi, Biochem. Z., **113**, 79 (1921)
Sparrow, male & female	10	0.022	.049	5.2	+21	Benedict & Fox, Pflugers Arch., **322**, 357 (1933)
Canary, male and female	43	0.0163	.036	5.2	+51	Benedict & Fox, Pflugers Arch., **322**, 357 (1933)

* = 10% deducted from original values in order to change standing to lying values.

** = 30% deducted from the original value (10% for standing & 20% for heat increment of feeding).

E = Data taken from equation relating basal metabolism to body weight for the particular species as given in Mo. Res. Bull. 166.

TABLE 13.2. Heat Production of Mature Animals of Different Species[1]

Animal	Weight		Heat production per 24 hours per					% Deviation Heat Product $\frac{\text{Obs.} - \text{Comp.}}{\text{Comp.}}$
			Animal[1] (Observed)	Kg	Sq. M. (mostly per 10 $W^{2/3}$)	$Kg^{.73}$	Animal[2] (Computed)	
	(gm.)	*(oz.)*						
(Dwarf mouse)	(8)	.28	(1.00)	125	278	34	(2.1)	(−52)
Canary	16.3	.57	4.9	301	762	99	3.6	+36
Albino mouse	21	.74	3.6	171	526	60	4.3	−16
Sparrow	22.5	.79	5.2	231	652	83	4.5	+10
Parrakeet	27.7	.98	6.3	227	688	86	5.2	+21
"Fat Mouse"	57	2.0	7.3	129	550	59	8.9	−18
Dove	150	5.3	17.2	115	609	69	18.0	−4
Pigeon	278	9.8	28.4	102	667	72	28.3	+0.4
Rat	400	14.1	33.2	83	672	65	36.9	−10
Guinea pig	410	14.5	35.1	86	707	67	37.6	−7
	kg	*lb*						
"Runt pigeon"	.522	1.15	46.3	89	714	74	44.9	+3
Hen	2.1	4.6	115	55	701	67	124	−7
Rabbit	2.6	5.7	117	45	619	58	145	−19
(Marmot)	2.65	5.8	(75)	28	421	37	(147)	(−49)
Cock	2.8	6.2	145	52	730	68	153	−5
"Wild birds"	3.0	6.6	172	57	827	77	161	+7
Cat	3.0	6.6	152	51	731	68	161	−6
Macaque	4.2	9.3	207	49	674	73	206	+0.5
Goose	5.0	11.0	272	54	930	84	234	+16
Dog	14.0	31	485	35	745	71	498	−3
Goat (doe)	36.0	79	800	22	734	58	994	−20
Chimpanzee	38.0	84	1090	29	964	77	1034	+5
Sheep	45.0	99	1160	26	917	72	1170	−0.9
Woman	56.0	124	1250	22	790	66	1373	−9
Man	65.0	143	1640	25	917	78	1531	+7
Sow	122	269	2400	20	974	72	2433	−1
(Boar)	(235)	518	(5700)	24	1499	106	(3915)	(+46)
Cow & Steer	500	1102	6200	12	1094	66	6817	−9
(Bull)	(600)	1323	(12100)	20	1890	113	(7786)	(+55)
Small horse	253	558	4588	18	1147	81	4138	+11
Large horse	703	1550	11895	17	1504	99	8742	+36
(Elephant)	(3672)	8095	(49000)	13	2060	122	(29300)	(+67)

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[1] From F. G. Benedict, "Vital Energetics": A study on comparative basal metabolism. Carnegie Inst. Washington, Pub. 503, 1938, pp. 175–6. The last 3 columns were computed by us.

[2] Computed by the writer from equation $Q = 72.18\, M^{.7317}$ which may be rounded to $Q = 72.2\, M^{.73}$. This equation does not include figures in parentheses. The standard error of estimate is +15% and −13%. The index of correlation is 0.998, and the coefficient of correlation of Cal/kg$^{.73}$ is 15%. If the figures in parentheses are not omitted, the equation is $Q = 69\, M^{.76}$, with standard error of estimate of +27% and −21%.

Table 13.3

Rubner's[1] classic tabulation indicates that heat production per kg small mature dog is larger than per kilo large one,but nearly the same per square meter surface area. We found the following least-squares equation for Rubner's data: $Q = 142M^{.612}$, with $+S_R = 5.7\%$ and $-S_R = 5.4\%$.

Dog	Body Weight (kg.)	Heat Production in Calories per 24 Hours		
		Per Kg	Per Sq. Meter Body Surface	Per $Kg^{.612}$
I	31.20	35.68	1036	136
II	24.00	40.91	1112	140
III	19.80	45.87	1207	146
IV	18.20	46.20	1097	142
V	9.61	65.16	1183	157
VI	6.50	66.07	1153	137
VII	3.19	88.07	1212	138

[1] Rubner, Max, "Ueber den Einfluss der Korpergrosse auf Stoff—und Kraftwechsel", *Z. Biol.*, **19**, 535 (1883).

Table 13.4a. Data on Total (Including Fecal) Nitrogen

Animals	Body wt (kg)	Total N (mg per day)	Ref. No.	Animals	Body wt (kg)	Total N (mg per day)	Ref. No.
Mouse	.0150	12.85	1	Rabbit	2.60	562	1
Mouse	.0165	13.74	1	Rats	.050	31.6	2
Mouse	.0167	13.75	1	Rats	.100	55.2	2
Rats	.100	56.4	1	Rats	.200	75.8	2
Rat	.123	51.2	1	Chickens	.720	237	2
Rat	.162	65.7	1	Chickens	.740	240	2
Rat	.168	78.8	1	Chickens	.760	250	2
Rat	.175	84.6	1	Chickens	.800	253	2
Rat	.202	75.6	1	Chickens	.800	230	2
Pigeon	.260	121	1	Chickens	1.60	434	2
Pigeon	.300	133	1	Chickens	1.80	454	2
Pigeon	.340	151	1	Chickens	2.00	291	3
Chicken	.910	218	1	Chickens	1.92	281	4
Rabbit	1.88	405	1	Chickens	2.25	475	4
Rabbit	2.15	463	1	Chickens	2.28	324	4

1. Terroine and Sorg-Matter, *Arch. Internat. Physiol.*, **29**, 121 ('27).
2. Terroine and Sorg-Matter, *ibid.*, **30**, 126 ('28).
3. Mitchell and Hamilton, *The Biochemistry of Amino Acids*, p. 539 New York ('29).
4. Ackerson, *et al.*, *Poultry Science*, **5**, 153 ('25).

Table 13.4b. Data on Endogenous Urinary Nitrogen, Plotted in Fig. 13.14.

Animals	Body Wt. (kg)	Urin. N (mg per day)	Ref. No.	Animals	Body Wt. (kg)	Urin. N (mg per day)	Ref. No.	Animals	Body Wt. (kg)	Urin. N (mg per day)	Ref. No.	Animals	Body Wt. (kg)	Urin. N (mg per day)	Ref. No.
Rats (2nd series)	.025	8.50	1	Rats	.233	43.8	3	Swine	109.	4005	11	Rats	.416	88.9	17
" " "	.027	8.64	1	"	.235	54.8	3	"	132.	4360	11	"	.425	78.0	17
" " "	.032	9.60	1	"	.238	59.5	3	Rats	.155	39.1	12	"	.433	111.1	17
" " "	.039	10.3	1	"	.240	51.3	3	"	.165	44.5	12	"	.435	91.1	17
" " "	.039	10.7	1	"	.246	48.6	3	"	.220	61.5	12	"	.444	105.4	17
" " "	.044	12.3	1	"	.254	55.8	3	"	.225	51.5	12	"	.454	116.8	17
" " "	.044	12.4	1	"	.255	55.8	3	Rabbits	1.80	319	12	"	.481	75.5	17
" " "	.045	11.3	1	"	.257	53.8	3	"	2.30	523	12	"	.488	81.8	17
" " "	.048	12.5	1	"	.263	53.9	3	"	2.45	676	12	"	.516	82.9	17
" " "	.050	12.5	1	"	.290	63.9	3	Dogs	7.0	685	12	"	.529	130.6	17
" " "	.050	14.3	1	"	.324	68.1	3	Swine	11.2	1188	13	"	.532	108.2	17
" " "	.059	16.8	1	Guinea pigs	.326	62.0	3	"	11.5	1230	13	"	.537	111.9	17
" " "	.078	18.7	1	" "	.378	66.5	3	"	12.5	1122	13	"	.050	10.9	18
" " "	.086	21.1	1	" "	.410	66.0	3	"	14.0	1302	13	"	.070	16.5	18
" " "	.220	29.0	1	" "	.425	71.0	3	"	14.0	1381	13	"	.090	20.4	18
" " "	.263	33.9	1	" "	.430	83.1	3	"	15.5	1415	13	"	.110	21.3	18
" " "	.284	34.7	1	" "	.435	78.2	3	Rabbits	1.48	314	14	"	.130	21.6	18
" " "	.315	45.7	1	" "	.481	88.7	3	"	2.40	454	14	"	.150	29.3	18
" " "	.340	40.8	1	" "	.482	83.3	3	"	2.45	426	14	"	.170	33.8	18
" " "	.357	41.1	1	" "	.500	80.0	3	"	3.00	468	14	"	.190	33.1	18
Rats (3rd series)	.042	12.0	2	Rabbits	1.61	180	3	"	3.60	274	14	"	.210	34.7	18
" " "	.044	12.0	2	"	1.68	231	3	"	4.39	659	14	"	.230	25.3	18
" " "	.051	13.5	2	"	1.90	241.4	3	Swine	11.5	1449	14	Rabbits*	1.21	130	19
" " "	.053	18.0	2	"	2.17	250	3	"	12.0	1361	14	"	1.49	164	20
" " "	.053	14.5	2	"	2.22	251.5	3	"	14.0	1415	14	"	1.76	249	21
" " "	.054	15.0	2	"	2.30	212.6	3	"	14.5	1280	14	Dogs*	12.2	1610	22
" " "	.065	21.0	2	"	2.40	274.6	3	"	17.0	2680	14	"	12.7	2200	22
" " "	.073	19.1	2	"	2.49	340.2	3	"	17.5	2430	14	"	13.1	1600	22
" " "	.082	22.5	2	"	2.51	340.0	3	"	12.0	1367	15	"	13.5	1830	22
" " "	.088	23.0	2	"	2.78	360.2	3	"	12.0	1498	15	"	18.5	1700	22
" " "	.092	24.0	2	Swine	67.2	2763	3	"	12.5	1563	15	Swine*	10.9	540	23
" " "	.099	22.0	2	"	68.0	3080	3	"	13.0	1915	15	"	14.3	960	24
" " "	.107	23.0	2	"	70.8	2464	3	"	14.0	1609	15	"	16.8	900	23
" " "	.109	19.5	2	"	75.0	2864	3	"	14.0	1769	15	"	17.7	1090	24
" " "	.115	23.0	2	"	79.2	3421	3	"	15.0	1839	15	"	19.5	1090	23
" " "	.120	32.0	2	"	11.5	1031	4	"	15.0	2112	15	"	22.2	1600	24
" " "	.140	28.0	2	"	12.5	726	4	"	15.0	2413	15	"	25.0	1320	25
" " "	.160	31.0	2	"	12.5	762	4	"	16.0	2271	15	"	26.3	1190	25
" " "	.177	38.0	2	"	13.5	1172	4	"	13.0	1646	16	"	37.2	1610	23
" " "	.203	45.0	2	"	16.0	1318	4	"	13.5	1325	16	"	38.1	1880	26
" " "	.220	44.0	2	"	21.5	1838	4	"	14.0	2146	16	"	38.1	2000	26
" " "	.240	62.0	2	Rats	.130	44.8	5	"	21.0	2219	16	"	38.5	1830	23
" " "	.250	42.0	2	"	.134	39.2	5	"	23.0	2513	16	"	40.0	1950	26
" " "	.319	52.0	2	"	.141	54.9	5	"	24.5	2573	16	"	41.0	1540	27
Rats (4th series)	.048	17.5	2	"	.150	42.5	5	Rats	.243	66	17	"	46.3	2230	24
" " "	.051	25.5	2	"	.151	56.0	5	"	.271	93	17	"	68.1	2650	23
" " "	.061	23.0	2	"	.153	47.5	5	"	.286	90	17	"	74.9	2610	23
" " "	.062	24.8	2	"	.157	61.3	5	"	.291	79.3	17	Sheep*	31.9	990	28
" " "	.064	33.0	2	"	.162	58.8	5	"	.294	81.9	17	"	33.1	1030	29
" " "	.069	29.8	2	"	.166	56.4	5	"	.310	84.3	17	"	35.0	2370	30
" " "	.076	32.3	2	"	.170	59.7	5	"	.310	96.3	17	"	35.0	1810	30
" " "	.082	18.5	2	"	.173	50.9	5	"	.321	68.3	17	"	38.0	2590	31
" " "	.084	33.0	2	"	.179	42.2	5	"	.322	71.7	17	"	40.0	[illegible]	[illegible]
" " "	[illegible]	24.4	2	"	[illegible]	[illegible]	[illegible]								

Rats (4th series)	.104	31.5	2	"	.186	69.8	5	"	.331	85.9	17	"	[illegible]	[illegible]	[illegible]
" " "	.108	34.4	2	"	.192	55.5	5	"	.339	97.7	17	"	43.5	2390	31
" " "	.120	28.5	2	"	.192	39.9	5	"	.339	107.8	17	"	43.5	1160	29
" " "	.125	52.0	2	"	.196	40.6	5	"	.340	108.3	17	"	44.1	1050	29
" " "	.125	37.0	2	"	.211	86.7	5	"	.347	77.2	17	"	45.0	2630	30
" " "	.126	31.5	2	"	.216	59.7	5	"	.349	93.6	17	"	45.0	2410	30
" " "	.142	29.0	2	"	.225	83.0	5	"	.353	89.8	17	"	47.0	3390	31
" " "	.172	40.0	2	"	.227	72.9	5	"	.355	94.8	17	"	54.0	2020	31
" " "	.203	62.0	2	"	.226	81.2	5	"	.356	75.4	17	Humans*	55.7	2700	32
" " "	.230	56.5	2	"	.278	69.0	5	"	.357	86.9	17	"	57.5	2420	33
" " "	.234	61.5	2	Swine	15.5	1474	6	"	.358	90.7	17	"	57.8	1990	34
" " "	.240	54.5	2	"	15.5	1526	6	"	.358	100.8	17	"	58.0	1840	35
" " "	.250	42.0	2	"	17.0	1635	6	"	.368	77.1	17	"	60.5	2130	34
" " "	.320	52.0	2	"	24.5	2402	6	"	.369	82.6	17	"	61.4	2250	36
Mice	.020	12.9	3	"	8.5	997	7	"	.374	88.3	17	"	62.4	3040	37
"	.022	15.4	3	"	9.0	725	7	"	.374	63.5	17	"	63.5	3120	38
"	.022	13.7	3	"	9.5	911	7	"	.375	98.4	17	"	64.0	2600	32
"	.024	16.0	3	"	9.5	960	7	"	.376	98.0	17	"	64.0	3800	32
"	.026	15.2	3	"	11.5	1131	7	"	.381	79.7	17	"	65.0	2510	38
"	.027	16.2	3	"	13.2	1336	8	"	.383	80.9	17	"	65.3	1580	39
"	.028	15.7	3	"	14.7	1490	8	"	.385	106.9	17	"	69.7	3760	37
"	.029	16.7	3	"	15.2	1414	8	"	.386	99.3	17	"	70.5	3500	32
"	.030	17.0	3	"	15.5	1527	8	"	.388	82.1	17	"	71.0	2890	40
Rats	.172	40.0	3	"	18.5	1431	8	"	.388	91.9	17	"	71.3	3340	38
"	.178	44.0	3	"	26.5	1162	8	"	.392	98.2	17	"	72.5	1750	41
"	.179	44.8	3	"	99	4907	9	"	.394	103.9	17	"	76.2	2980	42
"	.184	39.2	3	"	200	8498	9	"	.396	81.6	17	"	79.2	2930	40
"	.186	36.9	3	"	14.5	1587	10	"	.396	104.4	17	"	88.0	2010	43
"	.191	44.8	3	"	132	4724	10	"	.396	80.8	17	Cattle*	145	6480	44
"	.198	38.3	3	"	13.25	1333	11	"	.398	70.9	17	"	168	5030	45
"	.206	48.8	3	"	18.25	1706	11	"	.401	78.3	17	"	177	6330	45
"	.209	39.6	3	"	40.5	1559	11	"	.403	99.5	17	"	385	16320	46
"	.213	45.7	3	"	66.0	2328	11	"	.406	79.9	17	"	440	16400	46
"	.225	42.6	3	"	76.2	2157	11	"	.409	86.4	17	"	443	15000	47
"	.230	38.0	3	"	88.5	4124	11	"	.409	84.2	17	"	485	14000	47

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* From Mitchell's compilation given in Bull. 67 National Research Council ('29).

Table 13.5. Data on Creatinine Nitrogen Excretion.

Animals	No. of Trials or Animals	Body Wt. (kgs)	Creatinine N (mgs per day)	Ref. No.	Animals	No. of Trials or Animals	Body wt. (kgs)	Creatinine N (mgs per day)	Ref. No.	Animals	No. of Trials or Animals	Body wt. (kgs)	Creatinine N (mgs per day)	Ref. No.
Cattle Holstein fem.	1	75	750	1	Pigs	6	15.5	199	7	Humans	18	57.0	594	27
Cattle Holstein fem.	1	125	1500	1	Pigs	6	18.5	134	7	Humans	13	58.7	497	29
Cattle Holstein fem.	1	175	1460	1	Pigs	6	26.5	245	7	Humans fem.	26	58.7	340	30
Cattle Holstein fem.	4	225	2193	1	Pigs	7	8.0	85.6	8	Humans fem.	14	59.5	506	31
Cattle Holstein fem.	2	275	2860	1	Pigs	6	10.0	55.8	8	Humans	19	59.6	587	27
Cattle Holstein fem.	4	325	3388	1	Pigs	7	10.7	106	8	Humans	8	59.9	439	32
Cattle Bolstein fem.	3	375	4200	1	Pigs	7	11.0	118	8	Humans fem.	6	60.3	289	33
Cattle Holstein fem.	3	425	4450	1	Pigs	9	11.5	110	8	Humans	9	60.9	515	29
Cattle Holstein fem.	3	475	4857	1	Pigs	6	11.7	97.1	8	Humans	25	61.6	586	27
Cattle Jersey fem.	3	75	550	1	Pigs	4	11.7	98.6	8	Humans	6	62.1	303	34
Cattle Jersey fem.	5	125	1004	1	Pigs	9	12.0	128	8	Humans	7	63.3	579	29
Cattle Jersey fem.	5	175	1594	1	Pigs	8	12.0	119	8	Humans.	57	63.9	573	27
Cattle Jersey fem.	8	225	2190	1	Pigs	14	12.0	99	8	Humans	17	64.0	420	29
Cattle Jersey fem.	10	275	2635	1	Pigs	5	13.0	56.2	8	Humans	14	64.4	553	29
Cattle Jersey fem.	8	325	2898	1	Pigs	9	13.0	111	8	Humans	9	65.4	431	35
Cattle Jersey fem.	6	375	3450	1	Pigs	12	13.0	120	8	Humans	47	66.2	603	27
Rats mixed (low prot.)	6	0.037	0.67	2	Pigs	9	14.0	125	8	Humans	16	68.3	579	29
Rats mixed (low prot.)	8	0.063	1.00	2	Pigs	5	14.2	124	8	Humans male	6	68.4	638	33
Rats mixed (low prot.)	8	0.087	1.31	2	Pigs	13	14.5	98	9	Humans	56	68.5	671	27
Rats mixed (low prot.)	4	0.113	2.12	2	Pigs	10	132.0	1208	9	Humans	10	68.9	624	36
Rats mixed (low prot.)	8	0.137	2.25	2	Pigs	6	13.2	110	10	Humans male	12	69.2	521	29
Rats mixed (low prot.)	12	0.163	2.37	2	Pigs	7	18.3	131	10	Humans male	12	69.2	526	29
Rats mixed (low prot.)	13	0.187	2.98	2	Pigs	4	40.5	379	10	Humans	13	70.3	503	29
Rats mixed (low prot.)	14	0.213	3.57	2	Pigs	6	66.0	466	10	Humans	37	70.8	680	27
Rats mixed (low prot.)	11	0.237	3.74	2	Pigs	7	76.3	685	10	Humans	8	71.5	627	35
Rats mixed (low prot.)	18	0.263	4.03	2	Pigs	6	88.5	632	10	Humans	30	73.1	653	27
Rats mixed (low prot.)	10	0.287	4.35	2	Pigs	2	109.3	1175	10	Humans	24	75.4	596	27
Rats mixed (low prot.)	12	0.313	4.79	2	Pigs	7	132.0	880	10	Humans	22	77.7	600	27
Rats mixed (low prot.)	14	0.337	5.25	2	Pigs	8	11.2	93	11	Humans	14	80.0	593	27
Rats mixed (high prot.)	3	0.038	0.58	2	Pigs	6	11.5	91	11	Humans	13	82.3	727	27
Rats mixed (high prot.)	8	0.062	0.81	2	Pigs	8	12.5	102	11	Humans	12	84.6	733	27
Rats mixed (high prot.)	7	0.088	1.25	2	Pigs	4	14.0	113	11	Humans	12	86.5	573	29
Rats mixed (high prot.)	4	0.112	1.63	2	Pigs	6	14.2	142	11	Humans	16	89.0	666	29
Rats mixed (high prot.)	5	0.138	2.15	2	Pigs	6	15.5	162	11	Humans	5	89.2	750	27
Rats mixed (high prot.)	13	0.162	2.33	2	Pigs	6	11.5	80.7	12	Humans fem.	23	91.0	454	28
Rats mixed (high prot.)	9	0.188	2.80	2	Pigs	5	12.2	115	12	Humans	2	91.5	900	27
Rats mixed (high prot.)	15	0.212	3.08	2	Pigs	5	12.5	116	12	Humans	1	96.1	850	27
Rats mixed (high prot.)	12	0.238	3.42	2	Pigs	6	13.5	107	12	Humans	1	100.7	950	27
Rats mixed (high prot.)	24	0.262	3.75	2	Pigs	8	16.0	144	12	Rats	14	0.666	1.39	37
Rats mixed (high prot.)	18	0.288	4.08	2	Pigs	5	21.5	193	12	Rats	15	0.067	1.40	37
Rats mixed (high prot.)	9	0.312	4.75	2	Pigs	6	15.2	122	13	Rats	10	0.075	1.66	38
Rats mixed (high prot.)	5	0.338	5.05	2	Pigs	6	15.4	127	13	Rats	10	0.107	2.73	38
Rats mixed (high prot.)	5	0.362	5.15	2	Pigs	9	17.0	124	13	Rats	7	0.197	2.90	39
Rats mixed	2	0.071	1.10	3	Pigs	6	24.5	127	13	Rats	6	0.290	4.50	39
Rats mixed	2	0.093	1.62	3	Pigs	8	13.5	120	14	Rats	17	0.297	1.60	40
Rats mixed	2	0.114	1.84	3	Pigs	8	13.5	128	14	Rabbits	6	0.764	5.92	41
Rats mixed	2	0.138	2.17	3	Pigs	8	15.0	118	14	Rabbits	9	1.35	18.3	42
Rats mixed	2	0.159	2.71	3	Pigs	8	15.0	124	14	Rabbits	18	1.85	25.7	42
Rats mixed	2	0.172	3.19	3	Pigs	6	15.5	145	14	Rabbits	11	1.85	26.2	43
Rats mixed	2	0.180	3.56	3	Pigs	5	15.5	162	14	Rabbits	12	2.08	32.0	44

Mice	1	0.022	0.71	4
Mice	5	0.028	0.82	4
Rats	23	0.266	3.43	4
Guinea pigs	9	0.430	5.48	4
Rabbits	10	2.20	37.8	4
Pigs	5	72.0	5.25	4
Rats	1	0.155	4.42	5
Rats	1	0.165	4.16	5
Rats	1	0.220	5.67	5
Rats	1	0.225	5.82	5
Rabbits	1	1.80	17.0	5
Rabbits	1	2.30	23.0	5
Rabbits	1	2.45	30.0	5
Dogs	1	7.00	58.0	5
Rats	2	0.11	0.99	6
Rats	4	0.13	1.44	6
Rats	3	0.30	3.17	6
Pigs	4	8.00	58.4	6
Pigs	7	8.50	58.8	6
Pigs	5	9.00	66.2	6
Pigs	4	9.50	69.6	6
Pigs	4	9.50	78.9	6
Pigs	8	11.2	111	6
Rabbits	4	2.7	36	7
Rabbits	4	3.3	47.2	7
Pigs	6	13.5	161	7
Pigs	10	15.0	146	7
Pigs	10	15.0	159	7
Pigs	3	10.0	[illegible]	[illegible]
Humans	5	3.28	9.5	15
Humans	12	3.40	16.9	16
Humans	3	8.80	8.7	17
Humans	12	3.83	10.3	18
Humans	6	6.68	28.3	19
Humans	3	6.73	26.5	19
Humans	4	6.80	27.2	19
Humans	7	7.79	34.9	16
Humans	114	9.60	78.5	20
Humans male	3	14.0	82.2	21
Humans	4	14.4	64.5	22
Humans	1	16.0	81.5	23
Humans	6	17.1	72.9	20
Humans	4	17.9	96.9	22
Humans	8	18.5	133	24
Humans	10	19.0	89	25
Humans	10	22.3	173	24
Humans	16	25.2	181	24
Humans male	1	28.4	150	26
Humans	4	28.7	176	22
Humans male	1	30.0	90	26
Humans	1	33.5	301	23
Humans	1	38.0	239	23
Humans	2	45.5	650	27
Humans	2	52.4	500	27
Humans fem.	24	53.6	428	28
Humans	9	54.7	639	27
Humans	13	55.7	418	29
Rabbits	12	[illegible]	[illegible]	[illegible]
Rabbits	11	2.95	20.9	40
Guinea pigs	5	2.20	46.8	47
Fox	1	4.78	45.0	48
Coyotes	6	7.10	100	49
Coyotes	1	15.0	140	48
Dogs	49	3.17	28.2	50
Dogs	14	7.07	57.5	51
Dogs	2	7.44	76.4	52
Dogs	13	9.48	97.7	50
Dogs	4	9.59	43.1	40
Dogs	4	11.1	101	53
Dogs	3	11.7	121	54
Dogs	4	14.5	152	55
Dogs	3	18.0	93.6	40
Dogs	1	26.4	410	56
Pigs	3	18.1	156	57
Pigs	2	24.5	148	58
Pigs	6	31.5	337	59
Pigs	1	46.3	488	57
Sheep	5	57.4	324	60
Sheep	2	64.6	361	61
Sheep	5	82.0	651	60
Camel	1	515	3430	62
Steers	5	724	5160	63
Steers	4	707	5955	63
Steers	20	636	5107	63

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Table 13.6. Data on Neutral Sulfur Excretion.

Animals	No. of Trials or Animals	Body wt. (kgs)	Neutral Sulphur (mgs/day)	Ref. No.	Animals	No. of Trials or Animals	Body wt (kgs)	Neutral Sulphur (mg/day)	Ref. No.	Animals	No. of Trials or Animals	Body wt. (kgs)	Neutral Sulphur (mgs/day)	Ref. No.
Rabbits	9	2.52	20.8	1	Pigs	11	120	210	2	Pigs		21.5	52.8	4
Rabbits	8	3.25	16.0	1	Pigs	8	120	367	2	Humans	13	55.7	139.0	5
Rabbits	5	3.58	25.6	1	Pigs	10	120	427	2	Humans	10	57.5	223	5
Pigs	17	13.3	41.8	1	Rats	6	0.185	4.4	3	Humans	13	58.7	257	5
Pigs	6	14.5	37.8	1	Rats	6	0.185	4.5	3	Humans	9	60.9	207	5
Pigs	4	17.5	51.4	1	Rats	3	0.191	3.6	3	Humans	7	63.3	167	5
Pigs	9	18.0	44.0	1	Rats	6	0.192	1.3	3	Humans	17	64.0	246	5
Humans	6	57.5	130.8	1	Rats	4	0.195	1.3	3	Humans	14	64.4	154	5
Humans	6	57.5	131.0	1	Guinea pigs	3	0.445	2.3	3	Humans	16	68.3	166	5
Humans	5	57.0	60.3	1	Guinea pigs	2	0.445	1.2	3	Humans	13	70.3	185	5
Humans	4	65.0	94.3	1	Guinea pigs	6	0.712	5.3	3	Humans	12	86.5	234	5
Humans	4	65.0	86.8	1	Guinea pigs	6	0.725	5.7	3	Humans	16	89.0	302	5
Humans	5	65.0	84.8	1	Rabbits	5	0.780	8.3	3	Rabbits	3	2.27	17.0	6
Humans	2	68.0	108.0	1	Rabbits	5	0.785	7.6	3	Rabbits	7	2.59	22.6	7
Humans	5	69.0	90.6	1	Rabbits	2	1.782	9.7	3	Dogs	14	7.07	52.2	8
Rats	5	0.212	3.3	2	Rabbits	2	1.782	8.3	3	Dogs	11	7.23	80.6	9
Rats	5	0.220	2.7	2	Dogs	13	13.4	45.2	3	Dogs		9.6	50.0	10
Pigs	6	11.5	37.0	2	Dogs	12	14.6	33.4	3	Dogs		12.0	53.0	10
Pigs	6	11.5	38.0	2	Humans	3	3.25	8.9	3	Dogs	6	10.0	68.3	11
Pigs	6	11.5	45.0	2	Humans	8	14.5	27.1	3	Dogs	11	16.0	44.3	12
Pigs	9	16.0	51.0	2	Humans	8	19.5	30.4	3	Pigs	1	17.7	25.0	13
Pigs	8	16.0	58.0	2	Humans	6	42.2	74.5	3	Pigs	6	24.0	51.5	14
Pigs	8	16.0	27.0	2	Horses	6	330	1118	3	Pigs		28.7	199	15
Pigs	9	16.0	45.0	2	Horses	5	360	1130	3	Pigs		29.7	209	15
Pigs	7	16.0	48.0	2	Horses	4	384	834	3	Humans		69.5	98	16
Pigs		16.0	55.0	2	Pigs		11.5	38.0	4	Humans		80.0	121	16
Pigs	4	32.5	62.0	2	Pigs		12.5	31.0	4	Humans	8	64.0	120	17
Pigs	8	32.5	91.0	2	Pigs		12.5	36.0	4	Steers	19	636	236	18
Pigs	5	32.5	43.0	2	Pigs		13.5	40.0	4	Steers	4	707	1723	18
Pigs	8	120.0	137.0	2	Pigs		16.5	48.5	4	Steers	5	724	1339	18
Pigs	5	120.0	162.0	2										

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Various Factors.

Body Wt. Kgs.	Basal Metabolism Cals/Day		Endogenous Urin. Nitrogen (Mg/Day)		Protein Equivalent (Gms/Day)		Creatinine N (Mg/Day)		Neutral Sulphur (Mgs/Day)		Ratios Urinary N Excretion to Basal Metabolism (Mgs/Cals)				Creat. N / Urin. N %	Neutral Sulphur Urin. N Ratio	Cals. in Form Urin. N. Protein	
	Per Animal 1	Per Kg.	Per Animal 2	Per Kg.	Per Animal 3	Per Kg.	Per Animal 4	Per Kg.	Per Animal 5	Per Kg.	Urin. N	Protein Equivalent	Creatinine N	Neutral Sulphur			Per Day 6	% of Basal Metabolism
.01	2.40	240	5.30	530	.033	3.30	.205	20.5	.227	22.7	2.21	13.7	.085	.095	3.87	.0428	.132	5.50
.02	3.99	200	8.73	437	.055	2.75	.381	19.0	.379	18.9	2.19	13.7	.095	.095	4.36	.0434	.220	5.51
.03	5.37	179	11.7	390	.073	2.43	.549	18.3	.501	16.7	2.18	13.6	.102	.095	4.69	.0428	.292	5.44
.04	6.64	166	14.4	360	.090	2.25	.710	17.8	.633	15.8	2.17	13.5	.107	.095	4.93	.0439	.360	5.42
.05	7.82	156	16.9	338	.106	2.12	.867	17.3	.746	14.9	2.16	13.5	.111	.095	5.13	.0441	.424	5.42
.06	8.94	149	19.3	327	.121	2.02	1.02	17.0	.854	14.2	2.16	13.5	.114	.095	5.28	.0442	.484	5.41
.07	10.0	143	21.5	307	.134	1.91	1.17	16.7	.957	13.7	2.15	13.4	.117	.096	5.44	.0445	.539	5.39
.08	11.0	138	23.7	296	.148	1.85	1.32	16.5	1.06	13.3	2.15	13.4	.120	.096	5.57	.0447	.592	5.38
.09	12.0	133	25.8	287	.161	1.79	1.47	16.3	1.15	12.8	2.15	13.4	.123	.096	5.70	.0446	.644	5.37
.10	13.0	130	27.8	278	.174	1.74	1.61	16.1	1.25	12.5	2.14	13.4	.124	.096	5.79	.0450	.696	5.35
.20	21.6	108	45.8	229	.286	1.43	3.00	15.0	2.08	10.4	2.12	13.2	.139	.096	6.55	.0454	1.14	5.28
.30	29.1	97.0	97.0	205	.384	1.28	4.32	14.4	2.81	9.37	2.11	13.2	.148	.096	7.03	.0458	1.54	5.27
.40	36.0	90.0	75.5	189	.472	1.18	5.59	14.0	3.48	8.70	2.10	13.1	.155	.097	7.40	.0461	1.89	5.25
.50	42.4	84.8	88.6	177	.554	1.11	6.82	13.6	4.10	8.20	2.09	13.1	.161	.097	7.70	.0463	2.22	5.24
.60	48.5	81.0	101	168	.631	1.05	8.04	13.4	4.69	7.82	2.08	13.0	.166	.097	7.96	.0464	2.52	5.20
.70	54.3	77.6	113	161	.706	1.01	9.23	13.2	5.26	7.51	2.08	13.0	.170	.097	8.17	.0465	2.82	5.19
.80	59.9	74.9	124	155	.775	.969	10.4	13.0	5.81	7.26	2.07	12.9	.174	.097	8.39	.0468	3.10	5.17
.90	65.3	72.6	135	150	.884	.938	11.6	12.9	6.34	7.04	2.07	12.9	.179	.097	8.59	.0470	3.38	5.17
1.00	70.5	70.5	146	146	.913	.913	12.7	12.7	6.85	6.85	2.07	12.9	.180	.097	8.70	.0470	3.65	5.17
2.00	117	58.5	241	121	1.51	.755	23.6	11.8	11.4	5.70	2.06	12.9	.202	.097	9.79	.0473	6.04	5.16
3.00	158	52.7	321	107	2.01	.670	34.0	11.3	15.4	5.13	2.03	12.7	.215	.097	10.6	.0480	8.04	5.09
4.00	195	48.8	396	99.0	2.47	.618	44.0	11.0	19.1	4.78	2.03	12.7	.226	.098	11.1	.0482	9.88	5.07
5.00	230	46.0	465	93.0	2.91	.582	53.7	10.7	22.5	4.50	2.02	12.7	.233	.098	11.5	.0484	11.6	5.04
6.00	263	43.8	530	88.3	3.31	.551	63.2	10.5	25.8	4.30	2.01	12.6	.240	.098	11.9	.0487	13.2	5.03
7.00	294	42.0	593	84.7	3.71	.530	72.6	10.4	28.9	4.13	2.01	12.6	.247	.098	12.3	.0487	14.8	5.03
8.00	324	40.5	652	81.5	4.07	.509	81.8	10.2	31.9	3.99	2.01	12.6	.252	.098	12.5	.0489	16.3	5.03
9.00	354	39.3	710	78.9	4.44	.493	90.9	10.1	34.8	3.87	2.00	12.5	.257	.098	12.8	.0490	17.8	5.03
10.0	382	38.2	766	76.6	4.79	.479	100	10.0	37.6	3.76	2.00	12.5	.262	.099	13.1	.0491	19.2	5.02
20.0	636	31.8	1260	63.0	7.87	.393	186	9.30	62.9	3.15	1.98	12.4	.292	.099	14.8	.0499	31.5	4.95
30.0	856	28.5	1690	56.3	10.6	.353	267	8.90	84.9	2.83	1.97	12.4	.312	.099	15.8	.0502	42.4	4.95
40.0	1060	26.5	2080	52.0	13.0	.325	346	8.65	105	2.63	1.96	12.3	.326	.099	16.6	.0505	52.0	4.91
50.0	1250	25.0	2440	48.8	15.3	.306	423	8.46	124	2.48	1.96	12.2	.338	.099	17.3	.0508	61.2	4.90
60.0	1420	23.7	2780	46.3	17.4	.290	498	8.30	142	2.37	1.95	12.2	.351	.099	17.9	.0511	69.6	4.90
70.0	1590	22.7	3110	44.4	19.4	.277	571	8.16	159	2.27	1.95	12.2	.359	.099	18.4	.0511	77.6	4.88
80.0	1760	22.0	3420	42.7	21.4	.267	644	8.05	175	2.19	1.94	12.2	.366	.099	18.8	.0512	85.6	4.86
90.0	1920	21.3	3730	41.4	23.3	.259	716	7.96	191	2.12	1.94	12.1	.373	.099	19.2	.0512	93.2	4.85
100	2070	20.7	4020	40.2	25.1	.251	787	7.87	207	2.07	1.94	12.1	.380	.100	19.6	.0515	100	4.83
200	3450	17.3	6620	33.1	41.4	.207	1460	7.30	345	1.72	1.92	12.0	.423	.100	22.1	.0521	166	4.81
300	4640	15.5	8870	29.6	55.4	.185	2105	7.02	466	1.55	1.91	11.9	.454	.100	23.7	.0525	222	4.78
400	5730	14.3	10910	27.3	68.2	.171	2725	6.81	577	1.44	1.90	11.9	.475	.101	25.0	.0529	273	4.76
500	6750	13.5	12810	25.6	80.1	.160	3330	6.66	681	1.36	1.90	11.9	.493	.101	25.9	.0532	320	4.74
600	7715	12.9	14610	24.3	91.3	.152	3920	6.53	789	1.31	1.89	11.8	.508	.101	26.8	.0534	365	4.73
700	8640	12.3	16320	23.3	102	.146	4500	6.43	873	1.25	1.89	11.8	.521	.101	27.6	.0535	408	4.72
800	9530	11.9	17970	22.5	112	.140	5070	6.34	964	1.21	1.89	11.8	.532	.101	28.2	.0536	448	4.70
900	10390	11.5	19560	21.7	122	.135	5630	6.26	1050	1.17	1.88	11.7	.542	.101	28.8	.0537	488	4.70
1000	11220	11.2	21100	21.1	132	.132	6190	6.19	1140	1.14	1.88	11.7	.552	.102	29.3	.0540	528	4.70

1. Computed from equation $Q = 70.5M^{0.734}$.
2. Computed from equaton $Ur.N = 146M^{0.72}$.
3. Protein equivalent = endog. urin. nitrogen times 6.25.
4. Computed from equation $C.N. = 12.7M^{.896}$.
5. Computed from equation $N.S. = 6.85M^{.74}$.
6. Calorific equivalent = gm. protein × 4.

13.8: Appendix.

13.8.1: Fitting equation $Y = aX^b$ to data. As outlined in the introduction the equation

$$Y = aX^b \tag{13.2}$$

may be written

$$\log Y = \log a + b \log X \tag{13.3}$$

which has the same form as the linear equation

$$Y = a + bX \tag{13.4}$$

and that (13.3) yields a linear distribution of data on logarithmic coordinate paper, as (13.4) yields a linear distribution of data on arithmetic paper. The first procedure, then, is to plot the data on logarithmic coordinate paper to determine whether the function is logarithmic.

It is, moreover, very desirable to plot data in such manner as to give a linear distribution of the data, for two reasons: (1) the eye is extremely sensitive to deviations from a straight line, and the degree of closeness of the grouping of the data around the straight line is a simple index of the degree of the reliability of the data; (2) it is very much easier to draw an average straight line than a curve. With some experience, such an average line drawn free-hand may be nearly as good as one fitted by the method of least squares. The equation can then be fitted to the line drawn in by inspection. Two points are read from the line and the equation obtained by the method outlined at the end of this section.

The second procedure of fitting equation (13.3) to the data is by the method of least squares. The problem is to find the numerical values of b and of $\log a$ so that the sum of the positive and negative deviations (vertical differences between the data points and the line representing the resulting equation) is zero, and the sum of the squares of the deviations is a minimum.

Since the equation has two unknowns, we must have two equations (I and II) to solve it. These two "normal equations", are obtained by multiplying the equation first by the coefficient of $\log a$, then by the coefficient of b.

Multiplying the equation by 1, which is the coefficient of $\log a$, we get

$$\log Y = \log a + b \log X$$

Then we sum up all points, and get

$$\text{I. } \Sigma(\log Y) = N\ (\log a) + b\Sigma(\log X)$$

(The symbol Σ, Greek Sigma, stands for "sum of"; N represents the number of data points.) This is our first "normal equation", I.

Having obtained the first "normal equation", I, by multiplying the equation by the coefficient of $\log a$, we next proceed to get the second "normal equation", II, by multiplying it by the coefficient of b, namely by $\log X$. Multiplying by $\log X$ and summing, we get

$$\text{II. } \Sigma \log X \cdot \log Y = \log a\ \Sigma \log X + b\ \Sigma\ (\log^2 X)$$

This is our second "normal equation", II. The two "normal equations" that we must solve are, therefore,

$$\text{I. } (\log Y) = N \log a + b\ (\log X)$$

$$\text{II. } (\log X \cdot \log Y) = \log a\ (\log X) + b\ (\log^2 X)$$

The application of the method of least squares is illustrated on the following set of actual metabolism data.

From the above two "normal equations" we see that the values we need to calculate are:

$$(\log Y);\ (\log X);\ (\log X \cdot \log Y);\ (\log^2 X);\ N$$

which are shown in the following table:

Species	Body Wt. X kg.	log X	Metabolism Y Cal/day	log Y	log $X \cdot$ log Y	($\log^2 X$)	($\log^2 Y$)
Mouse	0.0276	−1.5591	5.0	0.6990	−1.08981090	2.43079281	0.48860100
Rat	0.226	−0.6459	23.6	1.3729	−0.88675611	0.41718681	1.88485441
Rat	0.351	−0.4547	32.3	1.5092	−0.68623324	0.20675209	2.27768464
Fowl	2.0	0.3010	112	2.0492	0.61680920	0.09060100	4.19922064
Sheep	42.7	1.6304	1105	3.0434	4.96195936	2.65820416	9.26228356
Man	70	1.8451	1700	3.2304	5.96041104	3.40439401	10.43548416
Pony	281	2.4487	4683	3.6705	8.98795335	5.99613169	13.47257025
Jersey Cow	420	2.6232	5865	3.7683	9.88500456	6.88117824	14.20008489
Beef Steer	700	2.8451	8910	3.9499	11.23786049	8.09459401	15.60171001
Elephant	3833	3.5835	30924	4.4903	16.09099005	12.84147225	20.16279409
Summations		12.6173		27.7831	55.07818780	43.02130707	91.98528765

The number of data points, N, is 10; ($\log^2 Y$) is given, to be used later in computing the standard error of estimate.

$$\text{I. } \Sigma\,(\log Y) = N \log a + b\,\Sigma\,(\log X)$$

$$\text{II. } \Sigma\,(\log X \cdot \log Y) = \log a\,\Sigma\,(\log X) + b\,\Sigma\,(\log^2 X)$$

$$\text{I. } 27.7831 = 10 \log a + 12.6173\, b$$

$$\text{II. } 55.07818780 = 12.6173 \log a + 43.02130707\, b$$

Dividing each equation by the coefficient of log a, we get:

$$\text{I. } 2.7783100 = \log a + 1.2617300\, b$$

$$\text{II. } 4.3652911 = \log a + 3.4097079\, b$$

We can now eliminate one of the unknowns, log a, by subtracting equation I from equation II

$$1.5869811 = 2.1479779\, b$$

$$\therefore b = 0.73882562$$

To solve for log a, we substitute the value of b in one of the above equations. Substituting in equation I,

$$2.7783100 = \log \mathrm{a} + (1.2617300)\ (0.73882562)$$

$$\log a = 2.7783100 - 0.9321984$$

$$\log a = 1.8461116;\ \text{antilog of } \log a = 70.2.$$

Inserting the numerical values of a and b in the original equation, we get

$$Y = 70.2\ X^{0.74}$$

which is the solution of the problem.

We now need a test to ascertain the scatter of the data points about the line of the above equation. This test is called the "standard error of estimate" the formula for which is*:

$$\mathrm{S}^2_{yx} = \frac{\mathrm{d}^2}{N'}$$

in which d represents a single deviation of the actual value of Y from the value computed from the equation, and N' is the "degrees of freedom". The "degrees of freedom" are the number of data points less the number of constants in the equation.

The following short-cut formula is more suitable for solving our problem:

$$S^2_{\log y \cdot \log x}\ \frac{\Sigma(\log^2 Y) - \log a\,\Sigma\,(\log Y) - b\,\Sigma\,(\log X \times \log Y)}{N'}$$

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* Ezekiel, M., "Methods of Correlation Analysis," 1930.

Substituting:

$$S^2_{\log y \cdot \log x} = \frac{91.98528765 - (1.8461116 \times 27.7831) - (0.73882562 \times 55.07818780)}{10 - 2}$$

$$= \frac{91.98528765 - 51.29070319 - 40.69317640}{8}$$

$$= \frac{0.00140806}{8} = 0.000176075$$

$$S_{\log y \cdot \log x} = 0.0133$$

This standard error is the difference between two logarithms, and since the difference between two logarithms is a ratio, we may express the standard error in per cent. To do this we must assume a base, such as 100, along the equation line, to work from. Taking 100 for our base line, the logarithm of 100 is 2.000. Adding the standard error to it we get 2.0133. The antilog of this is 103.1, which is 3.1 per cent above our assumed base.

The negative standard error in per cent will, of course, be smaller than the positive because of the principle of logarithms. Using the same base as before, but subtracting instead of adding

$$2.00 - 0.0133 = 1.9867$$

The same result would have been obtained had we chosen any other point on the equation line as our base. The standard error for the equation in per cent, is then

$$+S_R = 3.1 \text{ per cent}$$

$$-S_R = 3.0 \text{ per cent}$$

This value of the "standard error of estimate" means that two-thirds of the time the metabolism computed from this equation will agree with the observed metabolism within $+3.1$ per cent and -3.0 per cent.

When it is desired to compute not only the regression coefficients but also other statistical measures, the computations may be simplified* by reducing the sum of the squares and products of the observed values (in this case, of the logarithms of the observed values) to the sum of squares and products of deviations from the proper means.

Letting observed values be denoted by capital letters, and deviations from mean by small case letters, after the fashion of Snedecor†, the desired reductions may be effected as follows:

$$\Sigma \log X = 12.6173$$

$$\left(\frac{\Sigma \log X}{N}\right) = 1.26173$$

$$\left(\frac{\Sigma \log X}{N}\right) \Sigma \log X = 15.919626$$

$$\log^2 X = 43.021307$$

$$\Sigma \log^2 X = 27.101681$$

$$\Sigma \log Y = 27.7831$$

$$\left(\frac{\Sigma \log Y}{N}\right) = 2.77831$$

$$\log^2 Y = 91.985288$$

$$\left(\frac{\Sigma \log Y}{N}\right) \Sigma \log Y = 77.190065$$

$$\Sigma \log^2 Y = 14.795223$$

$$N = 10$$

$$\Sigma \log X \cdot \log Y = 55.078188$$

$$\left(\frac{\Sigma \log X}{N}\right) \Sigma \log Y = 35.054771$$

$$\Sigma \log X \cdot \log Y = 20.023417$$

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* Method suggested by Hudson Kibler.

† Snedecor, G. W., "Statistical Methods," 1937.

The regression coefficients, a and b, the standard error of estimate, $S_{\log y \cdot \log x}$ or $+S_{y \cdot x}$, and the coefficient of correlation, ρ may then be computed as follows:

$$\log Y = \left(\frac{\Sigma \log Y}{N}\right) + \frac{\Sigma \log x \cdot \log y}{\Sigma \log^2 x}\left[\log x - \left(\frac{\Sigma \log x}{N}\right)\right]$$

$$\log Y = 2.77831 + .738826 \log X - .93220 = 1.84611 + .738826 \log X$$

$$Y = 70.2\, X^{0.74}$$

$$S^2_{\log y \cdot \log x} = \frac{\Sigma \log^2 y - b(\Sigma \log x \cdot \log y)}{N-2} = \frac{14.795223 - 14.793821}{8}$$

$$= .00017525$$

$$S_{\log y \cdot \log x} = .01324$$

$$+S_{y \cdot x} = [(\text{antilog } .01324) - 1]100 = (1.031 - 1)100 = 3.1 \text{ per cent}$$

$$-S_{y \cdot x} = \frac{3.1}{1.031} = 3.0 \text{ per cent}$$

$$\rho^2 = \frac{b(\Sigma \log x \cdot \log y)}{\Sigma \log^2 y} = \frac{14.793821}{14.795223} = .99905$$

$$\rho = .9999+$$

If we wish to evaluate b by inspection from only two data points (see p. 402) as for example from the weights and metabolism of the mouse and the elephant, we may do so by the equation

$$b = \frac{\log Y_{(\text{elephant})} - \log Y'_{(\text{mouse})}}{\log X_{(\text{elephant})} - \log X'_{(\text{mouse})}}$$

$$= \frac{4.4903 - 0.6990}{3.5835 - 1.5591} = 0.737$$

Therefore, after taking logarithms on both sides and solving for b, we have,

$$Y : Y_1 = X^b : X_1{}^b$$

$$= \frac{\log Y - \log Y_1}{\log X - \log X_1}$$

There is some objection to fitting a logarithmic equation to data by the method of least squares, because it involves squaring logarithms. To throw some light on this problem Feldstein and Hersh* made a comparative study of the constants obtained by computing them from the original data, and from the logarithms of the data. They found that while the two methods gave very similar results, the use of the logarithmic method was much less laborious. They were unable to establish any "certain criterion . . . for deciding which of the two methods is to be preferred."

The standard error of the exponent, b, they proposed is

$$S_b = \pm \frac{1 - \rho^2}{N - 2} \cdot \frac{\sigma \log y}{\sigma \log x} = \pm \sqrt{\frac{N\Sigma(\log^2 y) - [\Sigma(\log y)]^2}{N\Sigma(\log^2 x) - [\Sigma(\log x)]^2}}$$

It should be noted, however, that Schmalhausen† antedated Feldstein and Hersh in publishing a least-square solution of the exponent, b, and formulas for the standard errors of b and intercept a, and also in defending the use of the least-square solution of the logarithmic form of the simple parabola we are interested in.

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* Feldstein, M. J., and Hersh, A. H., *Am. Naturalist*, **69**, 344, 610 (1935).

† Schmalhausen, I., *Arch. Entwickl. Mech. Organ.*, **124**, 82 (1931).

TABLE 13.8. Numerical Values of X^b.

X	$X^{.73}$	$X^{.75}$	$X^{2/3}$	$X^{.5}$	$X^{.6}$	$X^{.7}$	$X^{.8}$	$X^{.9}$
2000	256.9	299.1	158.7	44.7	95.6	204.5	437.3	935.2
1900	247.5	287.8	153.4	43.6	92.7	197.3	419.8	893.1
1800	237.9	276.4	148.0	42.4	89.8	190.0	402.0	850.7
1700	228.2	264.7	142.4	41.2	86.7	182.5	384.0	807.9
1600	218.3	253.0	136.8	40.0	83.6	174.9	365.8	765.1
1500	208.2	241.0	131.0	38.7	80.5	167.2	347.4	721.9
1400	198.0	228.9	125.1	37.4	77.2	159.3	328.8	678.4
1300	187.6	216.5	119.1	36.1	73.8	151.3	309.8	634.6
1200	176.9	203.9	112.9	34.6	70.4	143.0	290.6	590.6
1100	166.0	191.0	106.6	33.2	66.8	134.6	271.1	546.1
1000	154.9	177.8	100.0	31.6	63.1	125.9	251.2	501.2
900	143.4	164.3	93.2	30.0	59.2	116.9	230.9	455.8
800	131.6	150.4	86.2	28.3	55.2	107.7	210.1	410.0
700	119.4	136.1	78.8	26.5	50.9	98.1	188.8	363.6
600	106.7	121.2	71.1	24.5	46.4	88.1	166.9	316.5
500	93.4	105.7	63.0	22.4	41.6	77.5	144.3	268.6
400	79.3	89.4	54.3	20.0	36.4	66.3	120.7	219.7
350	72.0	80.9	49.7	18.7	33.6	60.4	108.5	194.8
300	64.3	71.1	44.8	17.3	30.6	54.2	95.9	169.6
250	56.3	62.9	39.7	15.8	27.5	47.7	82.9	143.9
200	47.8	53.2	34.2	14.1	24.0	40.8	69.3	117.7
150	38.8	42.9	28.2	12.2	20.2	33.4	55.1	89.9
125	33.9	37.4	25.0	11.2	18.1	29.4	47.6	77.1
100	28.8	31.6	21.5	10.0	15.8	25.1	39.8	63.1
75	23.4	25.5	17.8	8.66	13.3	20.5	31.6	48.7
50	17.4	18.8	13.6	7.07	10.5	15.5	22.9	33.8
25	10.5	11.2	8.55	5.00	6.90	9.52	13.1	18.1
10	5.37	5.62	4.64	3.16	3.98	5.01	6.31	7.94
9	4.97	5.20	4.33	3.00	3.74	4.66	5.80	7.22
8	4.56	4.76	4.00	2.83	3.48	4.29	5.28	6.50
7	4.14	4.30	3.66	2.65	3.21	3.90	4.74	5.76
6	3.70	3.83	3.30	2.45	2.93	3.50	4.19	5.02
5	3.24	3.34	2.92	2.24	2.63	3.09	3.62	4.26
4	2.75	2.83	2.52	2.00	2.30	2.64	3.03	3.48
3	2.23	2.28	2.08	1.73	1.93	2.16	2.41	2.69
2	1.66	1.68	1.59	1.41	1.52	1.62	1.74	1.87
1	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
.9	.926	.924	.932	.949	.939	.929	.919	.909
.8	.850	.846	.862	.894	.875	.855	.837	.818
.7	.771	.765	.788	.837	.807	.779	.752	.725
.6	.689	.682	.711	.775	.736	.699	.665	.632
.5	.603	.595	.630	.707	.660	.616	.574	.536
.4	.512	.503	.543	.632	.577	.527	.480	.438
.3	.415	.405	.448	.548	.486	.430	.382	.338
.2	.309	.299	.342	.447	.381	.324	.276	.235
.1	.186	.178	.215	.316	.251	.200	.158	.126
.09	.172	.164	.201	.300	.236	.185	.146	.114
.08	.158	.150	.186	.283	.220	.171	.133	.103
.07	.144	.136	.170	.265	.203	.155	.119	.091
.06	.128	.121	.153	.245	.185	.140	.105	.080
.05	.112	.106	.136	.224	.166	.123	.091	.067
.04	.095	.089	.117	.200	.145	.105	.076	.055
.03	.077	.072	.097	.173	.122	.086	.060	.043
.02	.058	.053	.074	.141	.096	.065	.044	.030
.01	.035	.032	.046	.100	.063	.040	.025	.016

13.8.2: Numerical values of $X^{0.73}$, $X^{3/4}$, $X^{2/3}$ corresponding to values of X: Sarrus and Rameaux, Bergmann, Rubner, Meeh and others assumed that the value of b is 2/3 in the equation relating metabolism, Y, to body weight, X. In our study of the relation between metabolism and body weight of mature animals of different species, we found the value of b is 0.73. Kleiber found the value of b to be near 3/4.

According to our proposal for relating metabolism to X^b, metabolism should be related to $X^{2/3}$, or $X^{0.73}$, or $X^{3/4}$, depending on which of the values of b one accepts. In this chapter, metabolism is related to $X^{.73}$, and the value of a, which might be termed specific metabolism, is computed from the equation $a = \frac{\text{Cal.}}{X^{.73}}$, which is of the order of 70.5 when X is body weight in kg, or 39.5 when X is body weight in pounds. Kleiber evaluates a from the equation $a = \frac{\text{Cal.}}{X^{3/4}}$, which is of the order of 72 when X is body weight in kilos.

To save time computing the values of $X^{.73}$, or $X^{3/4}$, or $X^{2/3}$, we present Table 13.8 giving a series of numerical values of X^b for corresponding values of X (body weight). If the desired values of X are not in the table, given values of X^b may be plotted against corresponding values of X, and the value of X^b read for the desired value of X.

Table 13.9. The numerical values of a and b in the formula surface area = a (weight)^b. The area is given in sq. meters, weight in kg. (see p. 360).

	a	b	Remarks
Dairy cattle	0.14	0.57	50 Holsteins, birth to maturity.
Dairy cattle	0.15	0.56	Av. of 46 Jerseys and 50 Holsteins, birth to maturity.
Dairy cattle	0.12	0.60	Av. of 482 Guernseys, Holsteins, Jerseys, Ayrshires, birth to maturity.
Beef cattle	0.13	0.56	Av. 341 Herefords and Shorthorns, males, females, and steers, birth to maturity.
Horses	0.10	0.64	
Swine	0.10	0.63	
Sheep	0.12	0.57	

Chapter 14

Metabolism and Pulmonary Ventilation in Relation to Body Weight During Growth

> The embryo has no surface if the word surface be used in the physiological sense intended to convey to the reader the idea of an area from which heat is dissipated. *J. Barcroft*

14.1: Definitions. Fig. 13.7 shows a remarkably constant ratio of basa metabolism to $W^{0.73}$ in *mature* animals of *different species*, including the enormous body-weight range of 0.02 to 4000 kg (mice to elephants).

Such constancy cannot be expected during *rapid growth* for several reasons. First, there may be a *work*-energy cost (in the thermodynamic sense) of growth not separable from the basal metabolic cost (Ch. 3) which, of course, changes with advancing age and growth rate. Secondly, early life is essentially poikilothermic (Ch. 11); the thermoregulatory mechanisms are not called upon to function during prenatal life, so that it requires some time to develop their functions postnatally. Thirdly, the neuro-endocrine system involved in the thermoregulatory control of the metabolic rate does not attain maximal functional level until relatively late in life. For instance, the sex endocrines, adrenals, and thyroid influence energy metabolism, yet they do not mature until after puberty (Ch. 17). The brain, which is also said to be involved in the control of metabolism (Chs. 13, 17), does not attain the maximal metabolic level until age about 20 years in man, and 30 to 50 days in the rat[1,2]; the situation is similar in the dog, cat, rabbit, and guinea pig. The muscular mass, which necessarily affects metabolism, increases in man from 25 per cent of the total body weight at birth to about 43 per cent at maturity.[3]

As regards surface area, the younger the organism the more rapidly the change in shape from the "simple" spherical to the complex form, including many bizarre structures (allantois and amniotic sacks, membranes, renal and other tubules, etc.), which serve as parts of the surface-area complex.

Extrapolating the metabolism-surface "law" to the earliest stages leads to a fabulous heat production sufficient to burn up the early embryo. Thus

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[1] Himwich, H. E., *et al.*, *Am. J. Physiol.*, **125**, 601 (1939); **134**, 281 (1941); **137**, 327 (1942); **142**, 544 (1944).

[2] Tyler, D. B., and Harreveld, A., Id., **136**, 600 (1942).

[3] Wilmer, H. A., *Proc. Soc. Exp. Biol. and Med.*, **43**, 545 (1940). Latimer, H. B., *Growth*, **8**, 218 (1944).

extrapolating the equation $Y = 70.5X^{0.73}$ (Fig. 13.7) yields the following fantastic values:

Weight (g.)	10	1	0.1	0.01	0.001	0.0001	0.000001
Cal/kg/day	246	455	848	1578	2939	5472	18980

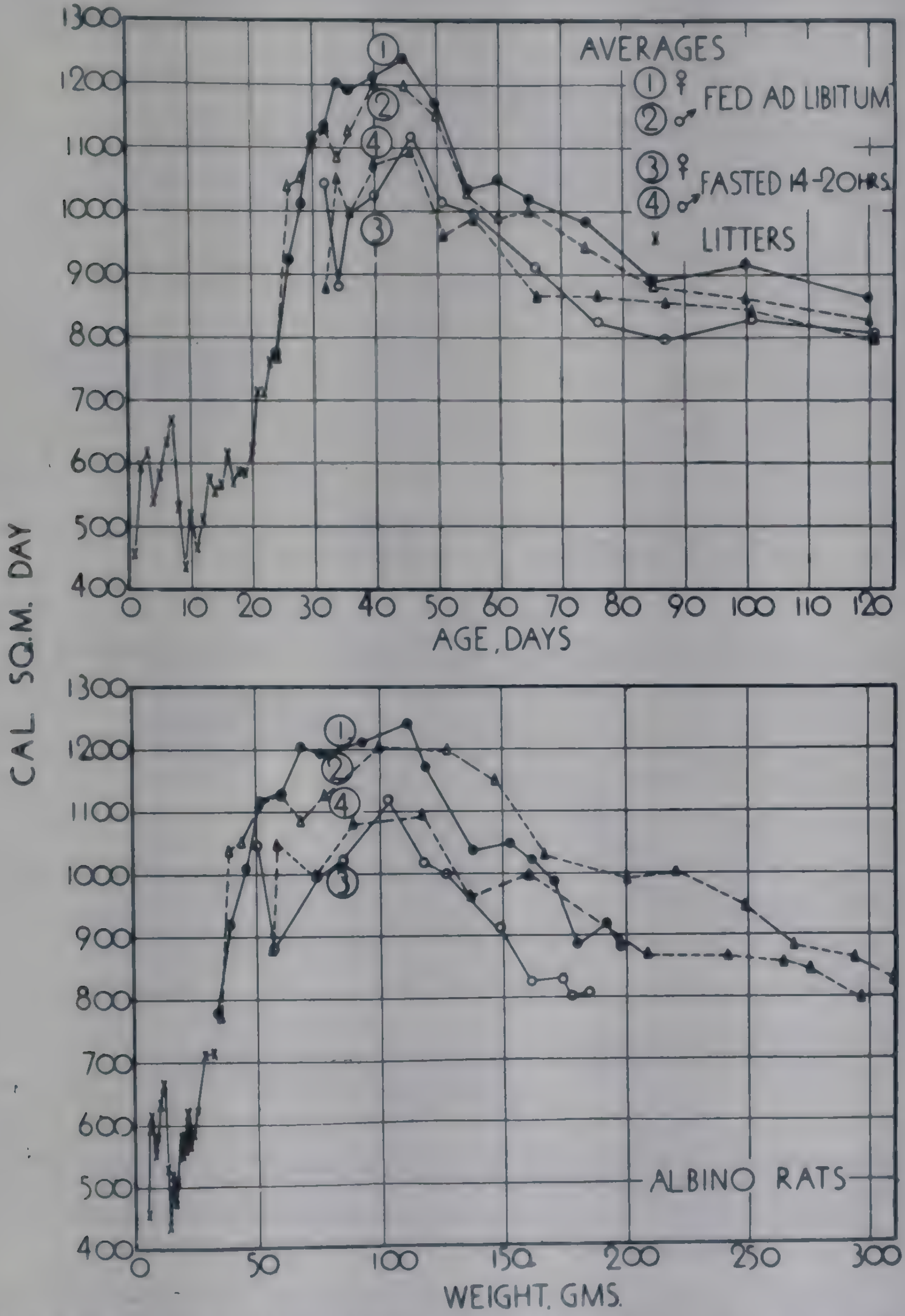

Fig. 14.1. Metabolism per unit surface area in rats as a function of age (upper section) and of weight (lower section). Plotted from Table 14.1.

The conclusion is that the metabolism per unit surface area, or per W^b (when b is $\frac{2}{3}$ to $\frac{3}{4}$), cannot remain constant during early growth, and that heat production per unit area must begin at a relatively low rate.

Because of the changing nature of the factors making up the heat-production complex in rapidly growing animals, we shall employ not the designation "basal metabolism", but "resting metabolism" when the metabolism is not post-absorptive and "fasting metabolism" when the resting metabolism is approximately post-absorptive. The following discussion is concerned with resting metabolism during *postnatal* growth—birth to sometime after puberty—in the form of age and weight curves of metabolism; and *prenatal* growth mostly in the form of total metabolism as function of birth weight.

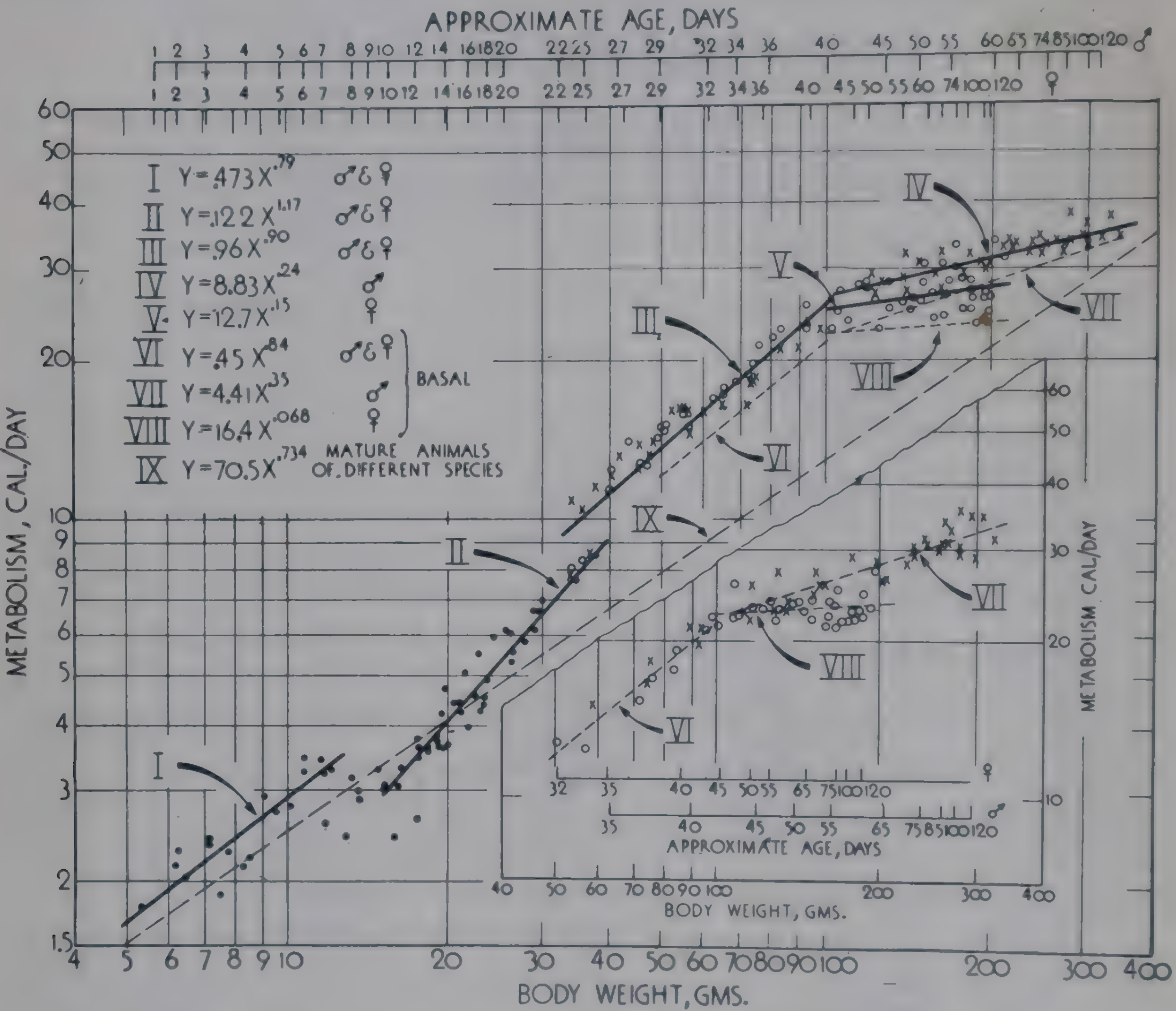

Fig. 14.2. The same data as 14.1, but the total metabolism per day is plotted against body weight on logarithmic paper. Basal data are shown in the insert. The other data represent *ad libitum* feeding. The curves for the various phases of growth represent the equation $Y = aX^b$ fitted to the data by the method of least squares.

14.2: Metabolism in relation to body weight in the white rat, with notes on cerebral metabolism. The measurements were made[4] at 30°C in an 8-chamber Regnault-Reiset volumetric apparatus (Fig. 12.11c) by the oxygen-consumption method. Windows in the chamber permitted activity observations; and as readings were taken every ten minutes for over an hour, observed activity could be eliminated from the averaging. The results, shown in Table 14.1a and Figs. 14.1 and 14.2, are thus metabolism during rest. Beginning with the thirty-second day, fasting (14 to 26 hours) as well as non-fasting data were secured. No attention was paid to the time of food intake preceding this age.

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[4] Kibler, H. H., and Brody, S., *J. Nut.*, **24**, 461 (1942).

As explained in the foregoing section and shown in Fig. 14.1, the metabolism per unit surface area rises; in this case it rises from about 400 Cal/sqm/day near birth to 1100 or 1200 at the age of 40 days or body weight of 100 g. Thereafter the metabolism declines to about 800 Cal/sqm/day at the age of four months or weight of 300 grams. After this, there is further decline associated with aging, discussed in Chapter 18.

This is typical of most age curves of metabolism, and as noted in the preceding section, it parallels in the rat the age curve of metabolism of the brain.[2] Such parallelism, however, does not hold for man. "In the human there is a slow rise in cerebral metabolic rate from birth to twenty years of age; it then remains constant until the senium when there is a progressive fall. The total human basal metabolic rate, on the other hand, is maximal at approximately two years of age. We are, therefore, left with different relationships for cerebral metabolic rate and basal metabolic rate in rat and in human".[5]

The explanation of this brain-body metabolic difference in rat and man is perhaps due to differences in the brain-body growth-rate difference. Man's brain may continue active growth for a relatively longer period than the rat's (Chs. 16, 17), and we believe (Ch. 3) that the metabolic rate is closely associated with the growth rate. The more rapid the growth rate, the higher the metabolic rate, partly because of the "work" of growth, but mainly because the rapidly growing tissue is more youthful, "more alive", than the slow-growing or non-growing. "Retardation of growth is old age" (C. S. Minot, see Ch. 18). It is particularly worthy of note (Table 14.1) that the metabolism per square meter tends to parallel the rise and decline of the growth rate (Ch. 3).

When *total metabolism* is plotted against *body weight* on *logarithmic* paper, as in Fig. 14.2 (which represents the same data as Fig. 14.1), the data appear to be distributed in four segments. To each of these segments the equation $Y = aX^b$ was fitted. The meaning of the first break, between segments I and II, is not clear, but data obtained by a different method on different animals and at a different time substantiate its reality. The break between segments II and III coincides with weaning, but may be due to a change in method of measurement, from entire litters in a chamber with no control over activity to individual rats in a chamber, with elimination of activity.

The final break, although it may not be as definite as pictured, seems to be real and associated with a change in percentage growth rate. Preceding the break (at about 100 g body weight) metabolism increases with the 0.8 to 0.9 power of body weight (a 1.0 per cent increase in weight is associated with an 0.8 to 0.9 per cent increase in metabolism); following the break, during the period of declining growth rate, metabolism increases with less than the 0.4 power of body weight. On a percentage basis, then, total metabolism increases more rapidly with weight during the period of rapid growth rate than during that of declining growth rate (Ch. 3).

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[5] Himwich, H. E., Personal communication.

Sex differences in metabolism at a given body weight become apparent after 45 days, and perhaps may likewise be attributed in part to differences in growth rates, the males being chronologically younger and growing more rapidly than the females of the same body weight.

Curve IX represents the relation of basal metabolism to body weight in mature animals of different species within the given weight range (Fig. 13.7). During the period of rapid percentage growth from weaning to 45 days, the metabolism (curve VI) of the rats is considerably higher than that of mature animals of different species; but as the rats approach their maximum body weights their metabolism approaches that of other species.

To summarize: when the resting metabolism of rats from birth to four months is plotted in terms of Calories per *unit area*, it rises steeply from birth (400 Cal/sqm/day) to the age of 40 days or to weight of 100 grams (1100 Cal/sqm/day for fasting and 1250 Cal/sqm/day for *ad libitum* feeding) and declines thereafter (800 Cal/sqm/day at four months). When plotted on logarithmic paper in terms of *total* metabolism against body weight, the distribution of the data indicates the presence of three breaks, one at the age of about ten days, one at weaning about three weeks, and one at about forty days. The first three segments have slopes ranging from 0.80 to 1.1 (the differential percentage rise in metabolism is 0.80 to 1.1 times as rapid as in body weight); the fourth segment has a slope of only about 0.2. The slope of the curves appears to vary directly with the percentage growth rate.

There is need for investigating the mechanisms behind these age changes; for correlating the age changes in metabolism with age changes in development of the oxidation-reduction enzymes[6], with age changes in ability to derive energy by glycolysis or fermentation (as contrasted to respiration, see Ch. 6), with age changes in homeothermy (discussed in Ch. 11), and with structural changes (Ch. 17).

A most interesting report is that by Himwich *et al.*[7] on age changes in tolerance to anoxia, hypoglycemia, fluoride, iodoacetate[8], and carbon monoxide.[9] While mature animals succumb in about three minutes, the average survival values for newborn animals in a pure nitrogen atmosphere is, in minutes, 50 for rats, 25 for cats, 23 for dogs, 16 for rabbits, 7 for guinea pigs. The longer survival value for the newborn is attributed by Himwich to lower brain metabolism, to early poikilothermicity, which makes smaller demands on oxygen, and especially to the fact that younger animals can and do obtain more energy by glycolysis.[2] One may suggest that the less highly developed brain of the immature animal is less sensitive to oxygen lack than the more highly developed brain of the mature. Fig. 14.3, after Himwich[7] *et al.*, illustrates the age changes in cerebral oxygen uptake and anoxic survival time in rats.

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[6] *Cf.* Needham, J., "Chemical Embryology," 1931, and "Biochemistry and Morphogenesis," 1943.

[7] Himwich, H. E., *et al.*, *Am. J. Physiol.*, **134,** 281 (1941); **135,** 387 (1942). See also Enzmann, E. V., and Pincus, G., *J. Gen. Physiol.*, **18,** 163 (1934), and Barcroft, J., *Proc. Roy. Soc.*, **118B,** 242 (1935); *Physiol. Rev.*, **16,** 103 (1936). Windle, W. F., "Physiology of the fetus," Philadelphia, 1940.

[8] *Cf.* Chapter 6. The sequence of anaerobic transformations, glucose phosphate → triose phosphate → phosphoglyceric acid → pyruvic acid → lactic acid, is blocked by fluoride at the phosphoglyceric acid stage and by iodoacetate at the triose phosphate stage.

[9] Cameron, J. A., *J. Cell. and Comp. Physiol.*, **18,** 379 (1941).

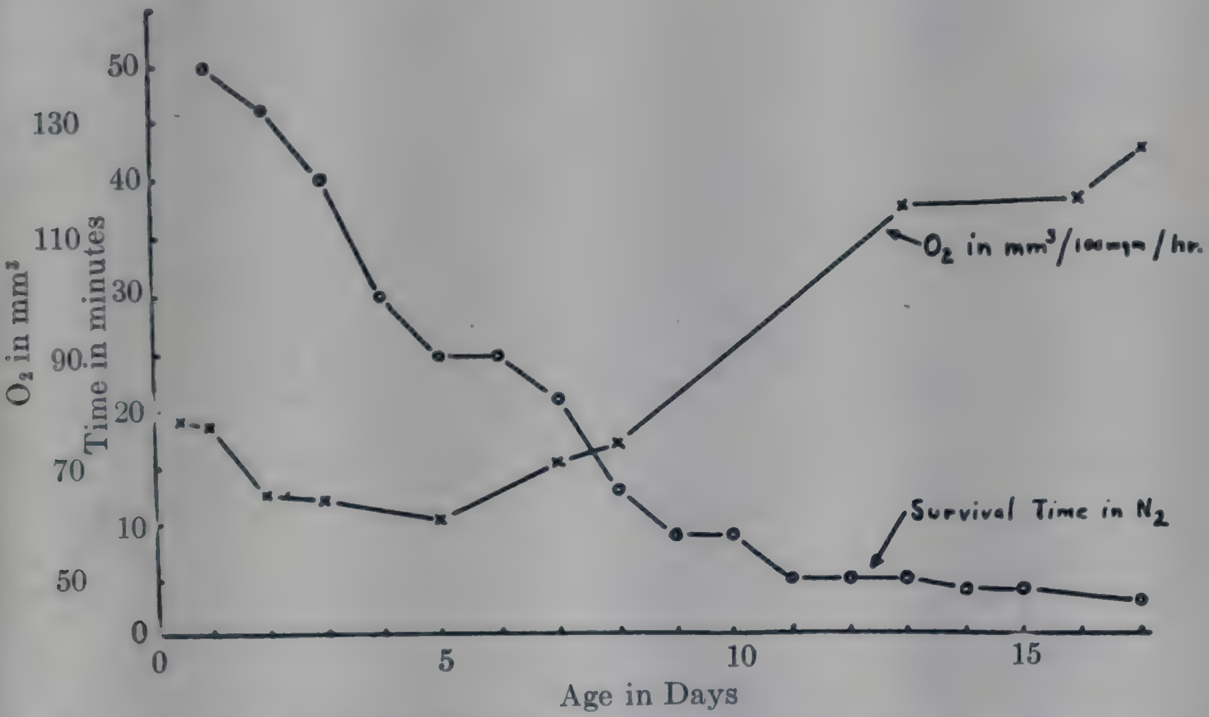

Fig. 14.3. Age changes in cerebral O_2 uptake and anoxic survival time in rats. From J. F. Fazekas, F. A. D. Alexander, and H. E. Himwich, *Am. J. Physiology*, **134,** 282 (1941).

14.3: Resting metabolism and pulmonary ventilation in dairy cattle. The picture relating resting metabolism to surface area and to weight of cattle during postnatal growth is, in general, similar to that of rats (Figs. 14.1 and 14.2) with the exceptions that (1) since cattle are born at a more advanced stage of physiologic development, they do not show some of the early postnatal features observed in the age curve of rats (Ch. 16); and (2) the resting metabolism per unit area (or similar reference base) in cattle is above that of rats.

The measurements were made before the regular morning feeding, 8 to 12 hours after the previous evening feeding, by the oxygen-consumption method illustrated in Figs. 12.3 and 12.4. Unlike humans, cattle take some 48 hours to reach post-absorptive condition, more or less time depending on age and other factors. These data are not, therefore, "basal" metabolism, but normal, early-morning metabolism at rest in a comfortable recumbent position. The data thus represent approximately minimum energy cost of maintenance, presumably including the energy expense of the *work* of growth and also some of the heat increment of feeding (Ch. 4).

Our numerical data[10] on the resting metabolism of Jersey and Holstein cattle are summarized in Tables 14.2 and 14.3. The resting metabolism *per square meter* per day is given in Figs. 14.4 and 14.5, and *total* resting metabolism as function of weight on logarithmic paper is given in Figs. 14.6 and 14.7.

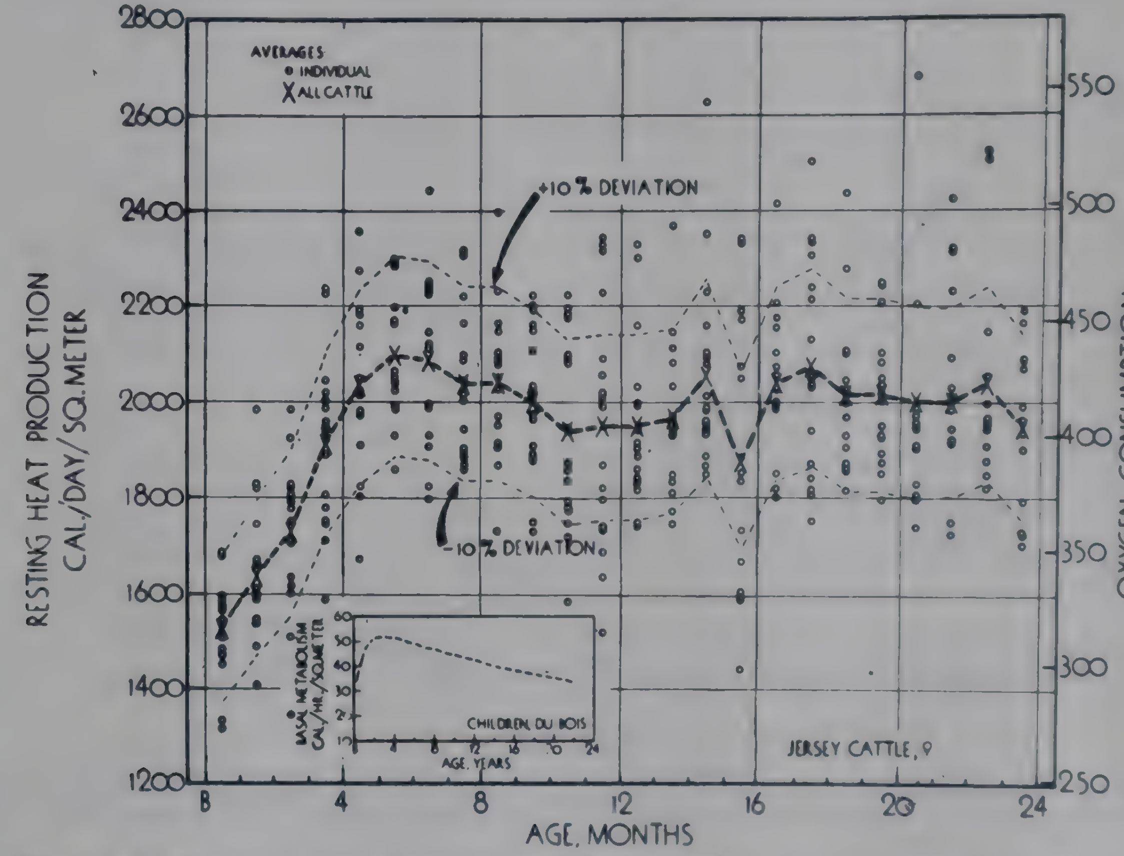

Fig. 14.4a. Resting heat production, Cal/sq m/day as function of age in Jersey cattle. The surface area, sq m, was computed from the equation $A = 0.15W^{0.56}$ (see Fig. 13.2 for details).

The resting metabolism *per unit surface area* rises in cattle from 1300 to 1400 Cal/sqm/day shortly after birth to about 2100 Cal/sqm/day at about five or six months (weight near 100 kg) and remains at this level for the duration of observation, until 24 months. The resting metabolism following this age is confused in dairy cattle (as managed under commercial conditions; these animals were *bona fide* members of a commercial dairy herd and not "experimental animals") by the heat increments of gestation and lactation.

The graph of the *total* metabolism as function of body weight on logarithmic paper, Figs. 14.6 and 14.7, shows a "break" at the age and weight correspond-

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[10] Brody, S., Kibler, H. H., and Ragsdale, A. C., Univ. Missouri Agr. Exp. Sta. Res. Bulls, 335 and 350, 1941–42.

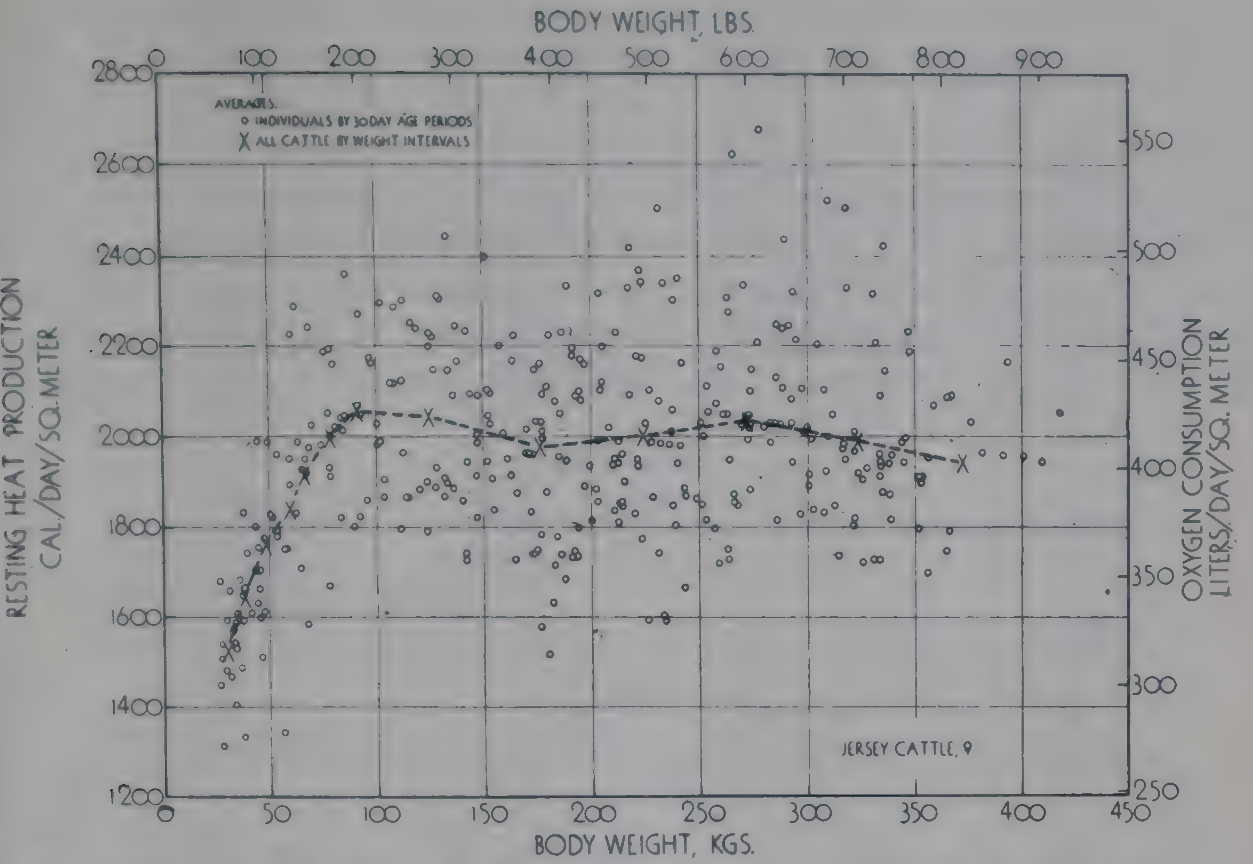

Fig. 14.4b. The same metabolism data as in Fig. 14.4a plotted against body weight.

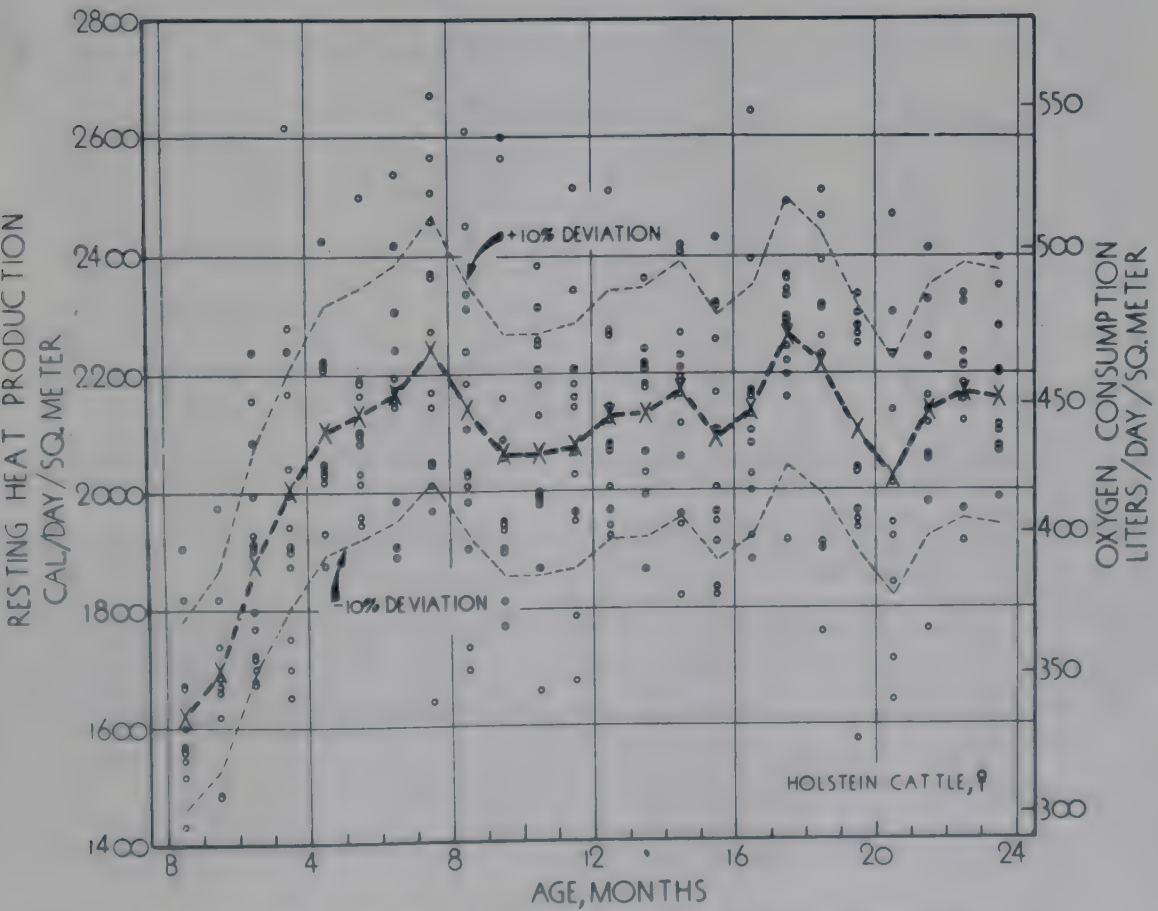

Fig. 14.5a. Similar data as in Fig. 14.4a but for Holstein cattle.

ing to maximum metabolism per unit area in Figs. 14.4 and 14.5, that is, at about five months or 100 kg. Unlike the rat age curve (Fig. 14.2), which shows three breaks, the cattle curve shows only the one break. The age curve of metabolism, as of growth (Ch. 16), of cattle is simpler than that of rats partly because cattle are born at a later developmental stage.

The equation $Y = aX^b$ was fitted by the method of least squares to each of the two segments. The heavy lines represent the equation, the light broken lines the standard error of estimate, designed by S_R, including between them two-thirds of the data. The light, broken lines III and IV represent

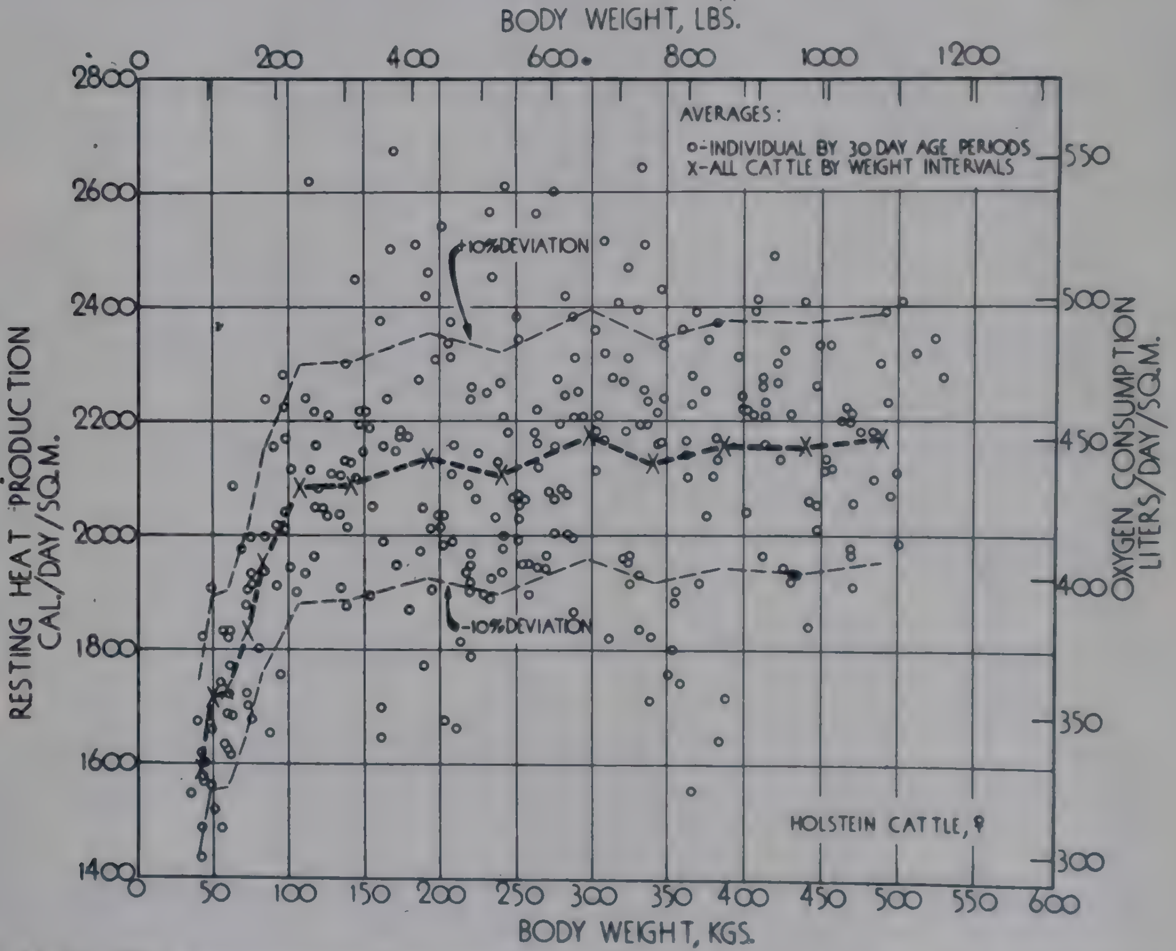

Fig. 14.5b. The same metabolism data as in Fig. 14.5a plotted against body weight.

the *basal* metabolism of *mature* animals of *different species* (mice to elephants), copied from Fig. 13.7.

Figs. 14.6 and 14.7 show that preceding the "break" at 5 to 6 months, or 200 to 300 lbs. live weight, the rise in resting maintenance energy cost is about 80 per cent of the rise in body weight (the value of the exponent b is 0.8); after the "break" the rise in metabolism is about 60 per cent of the rise in body weight (the value of b is 0.56 to 0.60), which is the same as the rise in surface area with increasing body weight (Fig. 13.2a and b: surface area $= 0.15W^{0.56}$).

The consistency of distribution of the data is indicated by the high index of

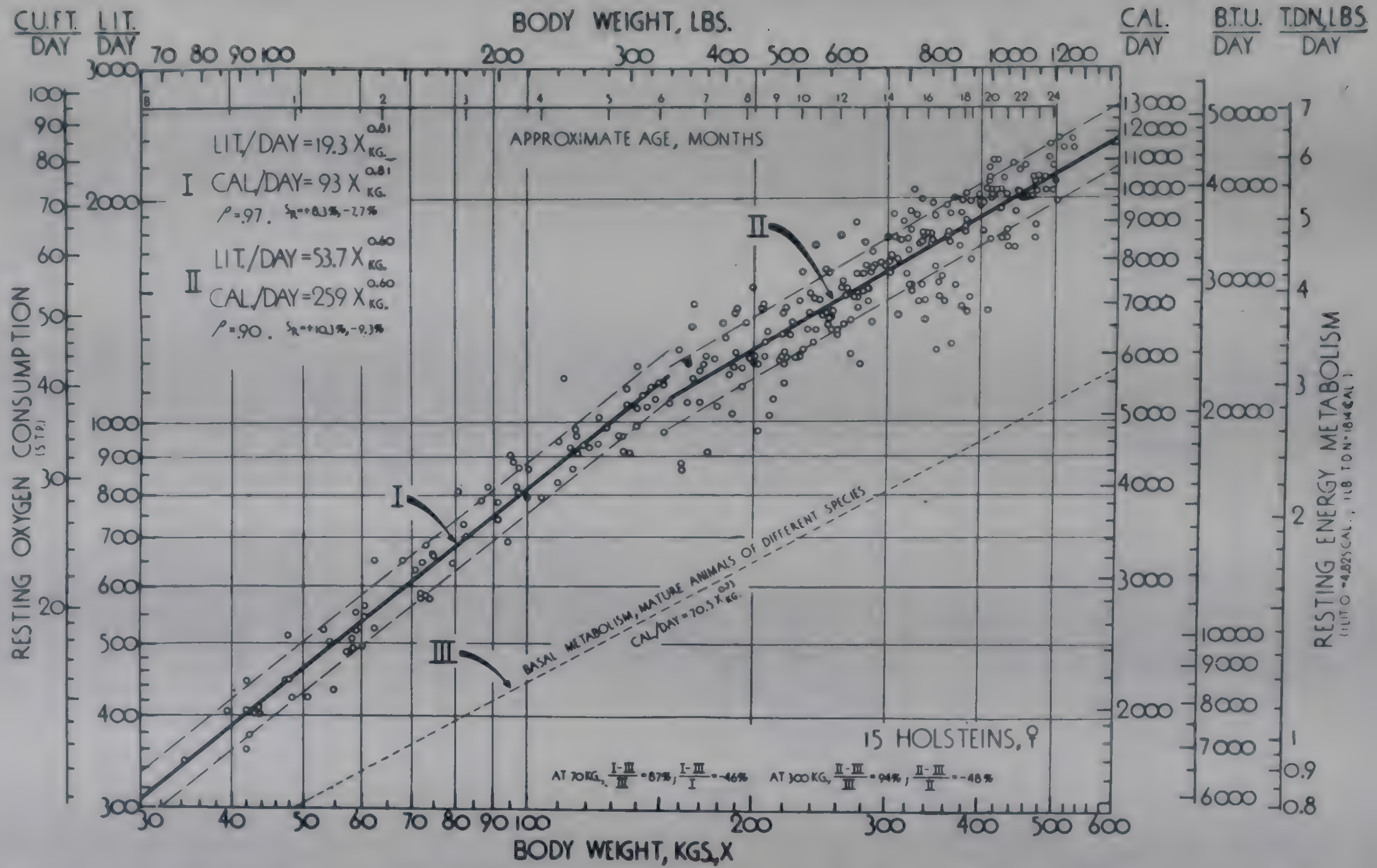

Fig. 14.6. Jersey cattle. Resting oxygen consumption (left axis) and heat production in terms of Cal., Btu, and TDN (right axis), plotted against body weight. The heavy line represents the equation $Y = aX^b$ with the values of a and b given on the chart, as well as of $\pm S_R$, which includes $\frac{2}{3}$ of the data. The lowest dash line—40% below the heavy line—represents the equation $Y = 70.5X^{.73}$ for *basal* metabolism (Cal/day vs. body weight in kg) of *mature* animals of *different* species.

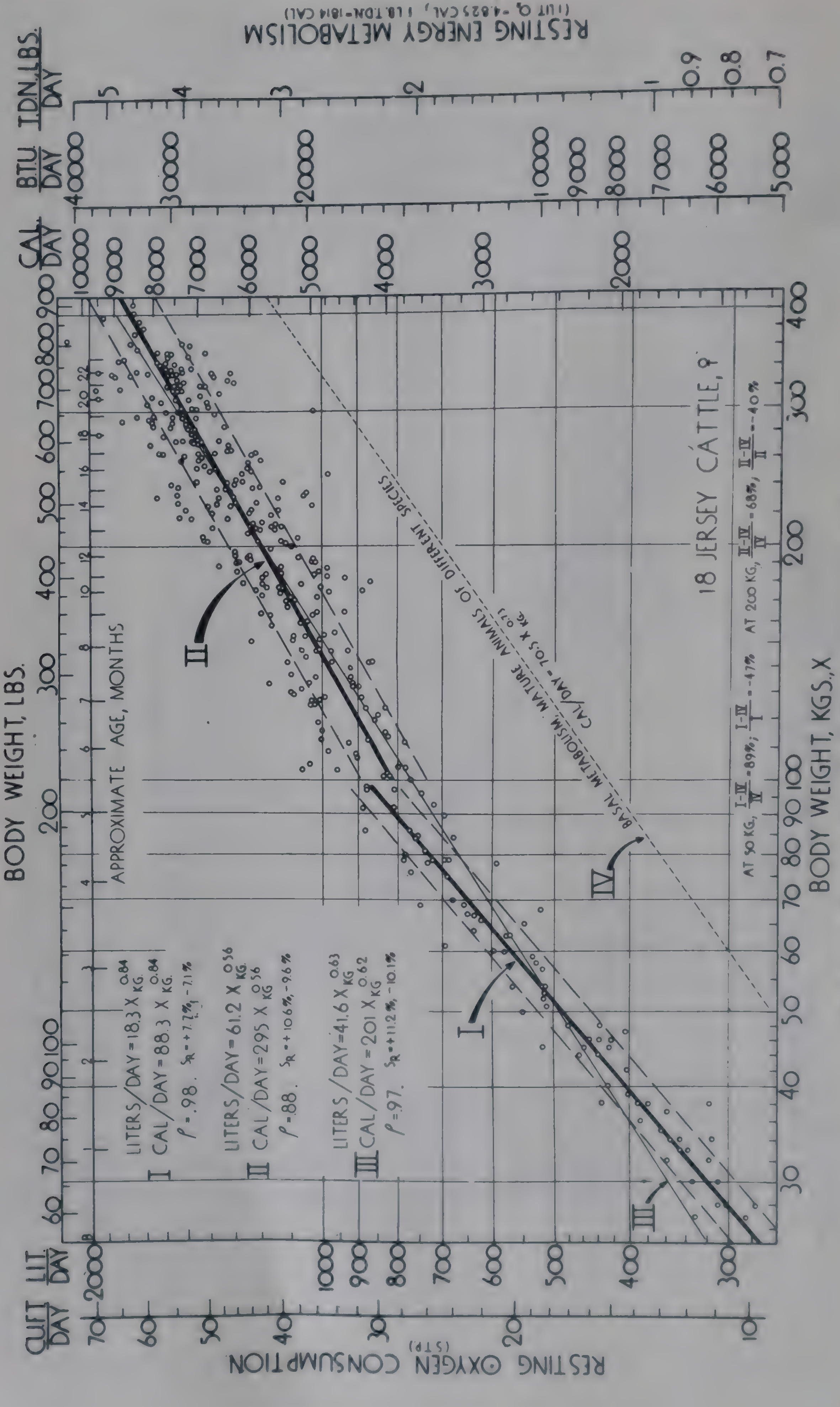

Fig. 14.7. Similar data as in Fig. 14.6 but for Holstein cattle.

correlation and the low standard error of estimate. The consistency is indeed remarkable, considering that the measurements were taken at all seasons on many animals born at different months and years and measured by different persons and with different equipment.

The *resting* (not fasting or "basal") metabolism of the *growing* animals is seen to be considerably above that of the *basal* metabolism of *mature* animals of different species. As indicated at the bottom of Figs. 14.6 and 14.7, the basal metabolism of mature animals of different species is 40 to 48 per cent below that of the resting metabolism of the growing cattle, or the resting metabolism of the growing cattle is 70 to 90 per cent above that of the basal metabolism of mature animals of different species. The resting metabolism curve of growing rats shown in Fig. 14.2 is nearer the basal-metabolism curve for mature animals of different species than is that of the cattle. The fact that relatively mature cattle and perhaps other ruminants have a higher metabolism per unit area than other species is known.[11]

Partly because of the interest in the ventilation problem by air-conditioning engineers, we have also collected data on the pulmonary *ventilation* (volume of air exhaled or inhaled per unit time) of these cattle. Such data are particularly useful for the light they throw on water vaporization, especially in slightly sweating or non-sweating animals, such as cattle. Although there is some question as to the saturation and temperature of the exhaled air, for practical purposes it is sufficient to assume that the exhaled air is saturated with moisture at the oral temperature of the species.[12] The pulmonary ventilation data, when combined with the oxygen-consumption data, thus furnish the ventilation or air-conditioning engineer practically all the needed data: air exhalation, oxygen consumption, carbon dioxide exhalation (virtually equivalent by volume to oxygen consumption) and water vaporization from the respiratory-oral system, which in non-sweating species is near the total water vaporized.

The ventilation rate tends to vary with the metabolic (oxygen-consumption) rate. In slightly sweating or panting animals such as cattle, the pulmonary ventilation rate serves a dual purpose, supplying oxygen and removing carbon dioxide and also fanning the pulmonary-oral surfaces, thus accelerating vaporization from these surfaces. In such species, therefore, the ventilation rate varies with temperature as well as with metabolic rate, and it is not surprising to find that the variability of the ventilation data is twice that of the metabolism data, as indicated in Figs. 14.8 and 14.9, representing on logarithmic paper ventilation rate as a function of live weight.

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[11] Ritzman, E. G., and Benedict, F. G., "Nutritional physiology of the adult ruminant," Carnegie Inst. Washington Pub., 494, 1938.

[12] The literature indicates that at the point of exhalation the air is 2° to 3° C below that of the mouth, and about 90 per cent saturated with respect to this exhalation temperature. In man, the usual oral temperature is assumed to be 37° C, the air at expiration 34° to 36° C, and the water content of the expired air is about 80 per cent of that of saturated air at 37° C, containing 0.032 to 0.037 g. H_2O per liter expired air. See Newburgh, L. H., and Johnston, M. W., *Physiol. Rev.*, **22**, 1 (1942).

Because of the high variability of ventilation data, no attempt was made to analyze the curve in two segments, and the equation $Y = aX^b$ was "forced" on the data by the method of least squares. The slope, b, of the resulting curve is seen in Figs. 14.8 and 14.9 to be 0.72 for the Jersey cattle and 0.77 for the Holstein cattle, which are reasonable values.

A surprising feature of Tables 14.2 and 14.3 is the low oxygen decrement in the expired air, about 2 per cent, much below that in man. Direct analysis of expired air (the values in Tables 14.2 and 14.3 are computed from the ventilation rate and from oxygen consumption) yields higher values; in one analysis on a six-year old Guernsey cow the results were 2.4 per cent oxygen deficit immediately after feeding and 2.2 per cent after a 48-hour fast. The use of the oxygen-spirometer method reduces the apparent oxygen deficit in expired air[13], but not enough to explain the low value for the oxygen deficit. Carpenter[14] suggested that in these (slightly sweating or non-sweating)

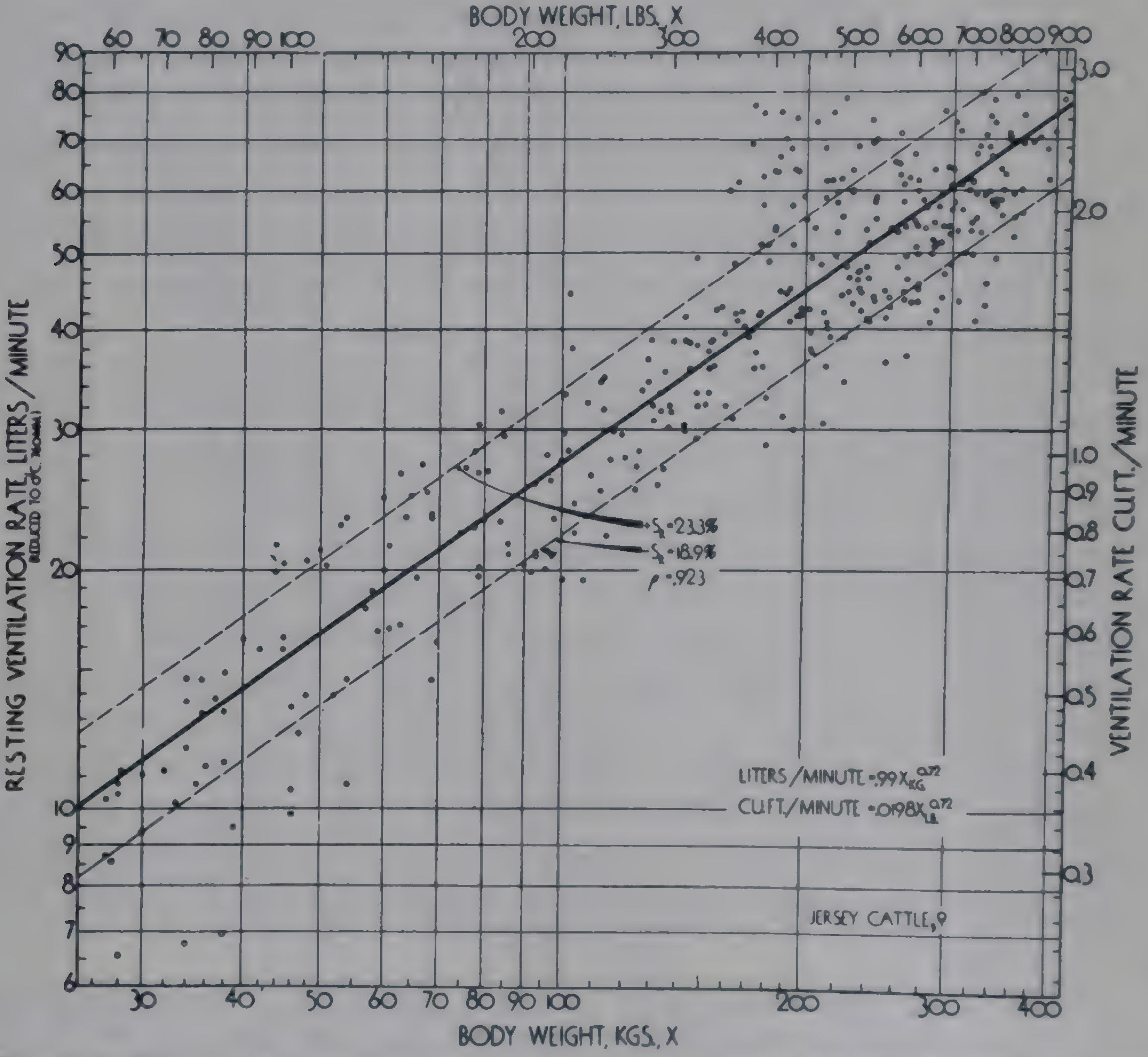

Fig. 14.8. Pulmonary ventilation rate (volume of air expired or inspired per minute) plotted against body weight. The heavy line represents the fitted equation $Y = aX^b$, the dash lines, the standard error of estimate, S_R.

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[13] Carpenter, T. M., *Boston Med. and Surg. J.*, **181**, 334 (1919), reported a ventilation rate (for man) of 6.32 liters per minute for closed-circuit apparatus and 5.38 liters per minute for open-circuit.

[14] Personal communication.

animals "the water elimination from the skin is so low that in order for the heat to be eliminated by way of vaporization of water there has to be a tremendous increase in lung ventilation" with consequent decrease in oxygen deficit in the expired air. We also have good data indicating that the larger the animal, the lower the ratio of oxygen to consumed air inhaled.

It is interesting to compare, by way of conclusion, the metabolism of the small Jersey and larger Holstein. This is done in Fig. 14.10. After the age of about six months Holstein heifers have a resting metabolism of, on the average, 2140 Cal/sqm/day; Jersey heifers, 2000 Cal/sqm/day. While these breed differences are relatively slight, they are statistically significant. The higher metabolism per unit surface area of the Holsteins *at given ages* (lower left chart) may be due to their more rapid growth rate. There is considerable evidence indicating that the heat production increases with increasing growth rate (Ch. 3).

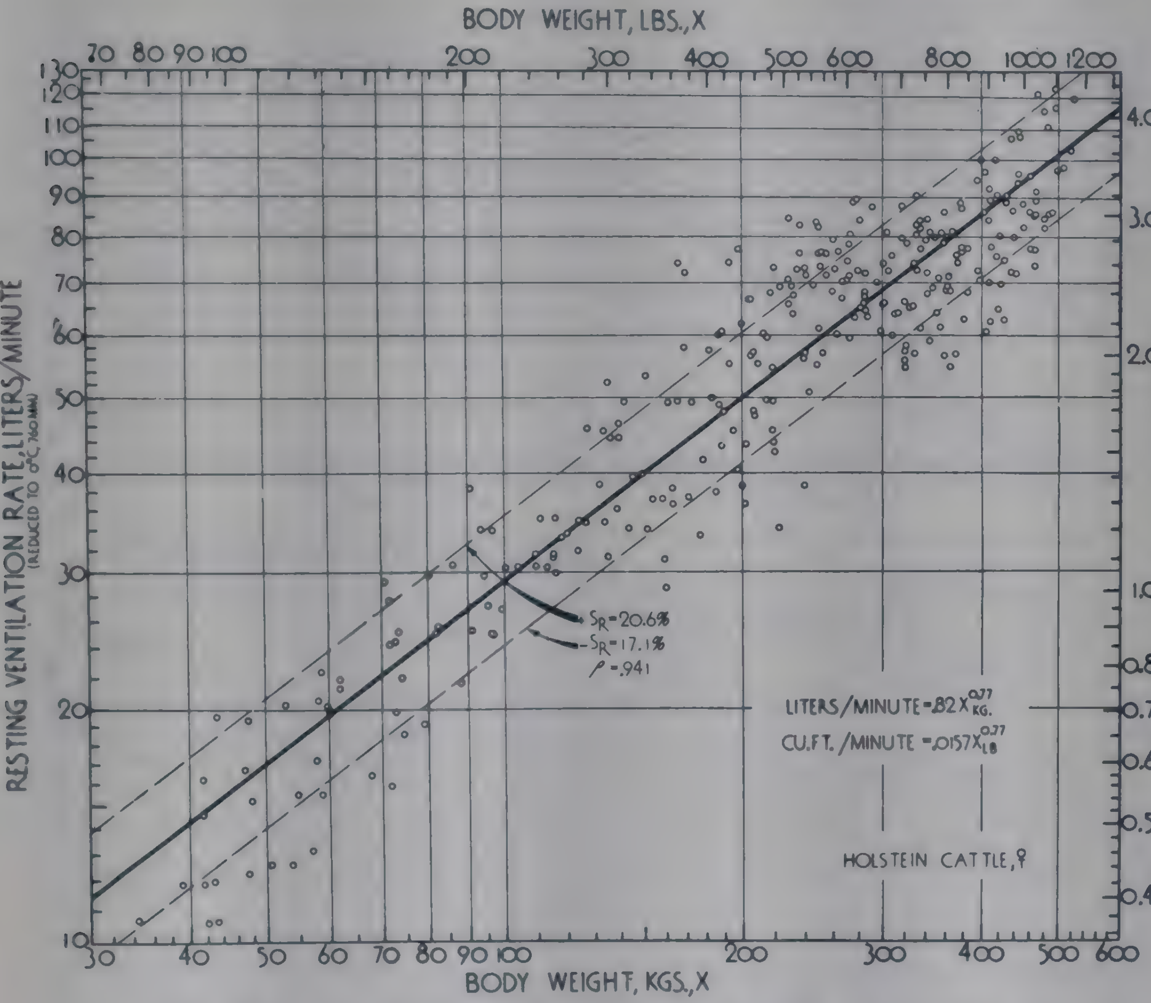

Fig. 14.9. Ventilation rate as in Fig. 14.8 but for Holstein cattle.

When plotted against *body weight*, on the other hand, the metabolism per unit surface area and per animal appears to be greater in the Jerseys prior to about 100 kg body weight (lower-right and upper-left curves). This may be due to the fact that at a given body weight the Jersey is physiologically older than the Holstein, and, as indicated in the charts, the metabolism per unit surface area (and per animal) rises with increasing age up to about six months, or up to about 100 kg body weight.

The higher Holstein ventilation rate at given body weights (upper-right curve) may perhaps be explained by the higher Holstein heat production (lower-right curve): ventilation rate is adjusted not only to the need for oxygen but also to the need for heat dissipation, since ventilation is an important method of heat dissipation in cattle and other non-sweating animals.

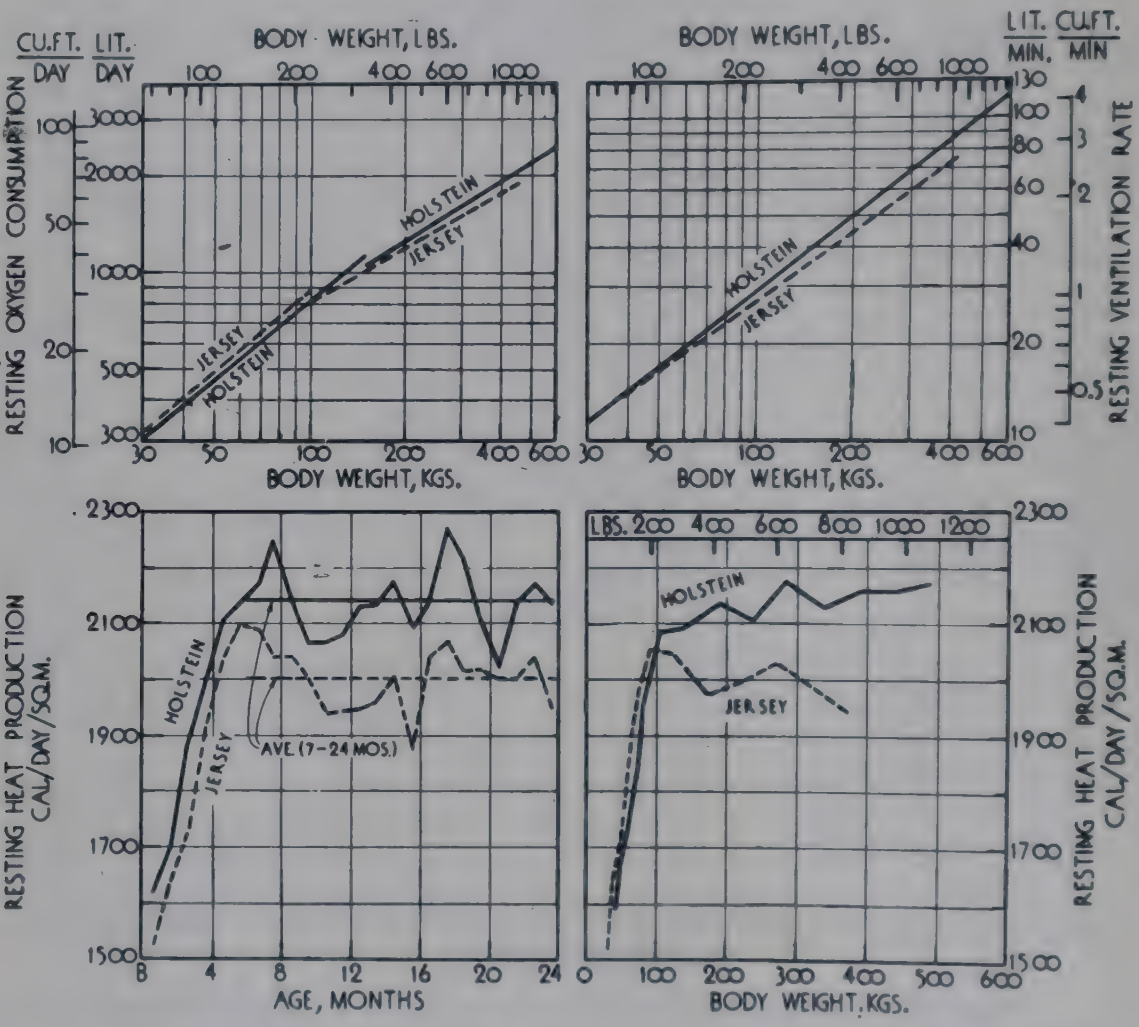

Fig. 14.10. Comparison of metabolic and ventilation rates in Jersey and Holstein cattle.

To summarize: the resting metabolism per unit area in dairy cattle rises from birth to puberty and remains roughly constant until the age of 24 months. The general age picture of metabolism per unit area is not unlike that for rats, but the changes are less extensive because of the more advanced physiologic age of cattle at birth. When total metabolism is plotted against weight on logarithmic paper the slope of the curve is about 0.8 prior to the break at 5 to 6 months, and 0.56 to 0.60 after this age, which means that following six months the metabolism per unit area is practically constant. The resting metabolism of growing cattle per unit area is considerably above that of growing rats or man. The ventilation rate of growing cattle increases with approximately the 0.7 power of body weight.

14.4: Resting metabolism in goats. Goats tend to be seasonal breeders, usually conceiving in October or November (the gestation period is 151 days). Goats are, moreover, very sensitive to changes in temperature, pasture, and other conditions associated with changes in season, all of which are reflected in the metabolic rate (Fig. 8.12a). The births of the 22 goats we investigated[15] were distributed throughout the year, with consequent individual differences in the slope due to seasonal and related influences. The slope relating resting metabolism to body weight ranged from 0.51 to 1.0.

Because of this variability no attempt was made to analyze the goat data with respect to the presence of segments as was done for rats and cattle. The equation $Y = aX^b$ was simply "forced" on the data by the method of least squares giving slopes (values of the exponent b) ranging from 0.50 to 0.72. It may be recalled that after the age of six months the slope of the curve for cattle is 0.60 (Figs. 14.6 and 14.7), quite close to the average of 0.64 for the goats.

The slope for all the females was 0.64; for all the males, 0.68; for all the Toggenberg goats (males and females), 0.67; for all the Angoras (males and females), 0.56.

We did not measure the surface area of the goats and found no surface-area data in the literature; therefore, no charts relating metabolism to surface area are given.

The metabolism for given individuals may be estimated from the following prediction values or from the equations.

Body Wt. (lbs)	Body Wt. (kg)	Resting metabolism (Cal/day)	Body Wt. (lbs)	Body Wt. (kg)	Resting metabolism (Cal/day)
4	1.8	240	45	20.4	1136
6	2.7	312	50	22.7	1215
8	3.5	375	60	27.2	1366
10	4.5	432	70	31.8	1508
12	5.4	486	80	36.3	1643
14	6.4	537	90	40.8	1772
16	7.2	585	100	45.4	1896
18	8.2	631	110	49.9	2016
20	9.1	675	120	54.4	2132
25	11.3	779	130	59.0	2244
30	13.6	875	140	63.5	2353
35	15.9	967	150	68.0	2460
40	18.1	1053	154	70.0	2502

Breed	Equation
Toggenberg males	Cal. = 88.5 $\text{lb}^{0.710}$ or 155 $\text{kg}^{0.710}$
Toggenberg females	Cal. = 88.8 $\text{lb}^{0.663}$ or 150 $\text{kg}^{0.663}$
Angora males	Cal. = 120 $\text{lb}^{0.596}$ or 192 $\text{kg}^{0.596}$
Angora females	Cal. = 140 $\text{lb}^{0.504}$ or 209 $\text{kg}^{0.504}$

[15] Mo. Agr. Exp. Sta. Res. Bull. 291, 1938.

The estimates here given for the *resting* metabolism of *growing* goats are considerably above the *basal* metabolism values published by Benedict *et al.*[16] for more mature animals.

14.5: Resting metabolism and pulmonary ventilation in horses. It was more difficult to get young horses than cattle to rest during the metabolism measurements. This may explain the differences in distribution between the horse and cattle data, especially when plotted in terms of metabolism per unit area as function of age or weight, shown in Fig. 14.11.

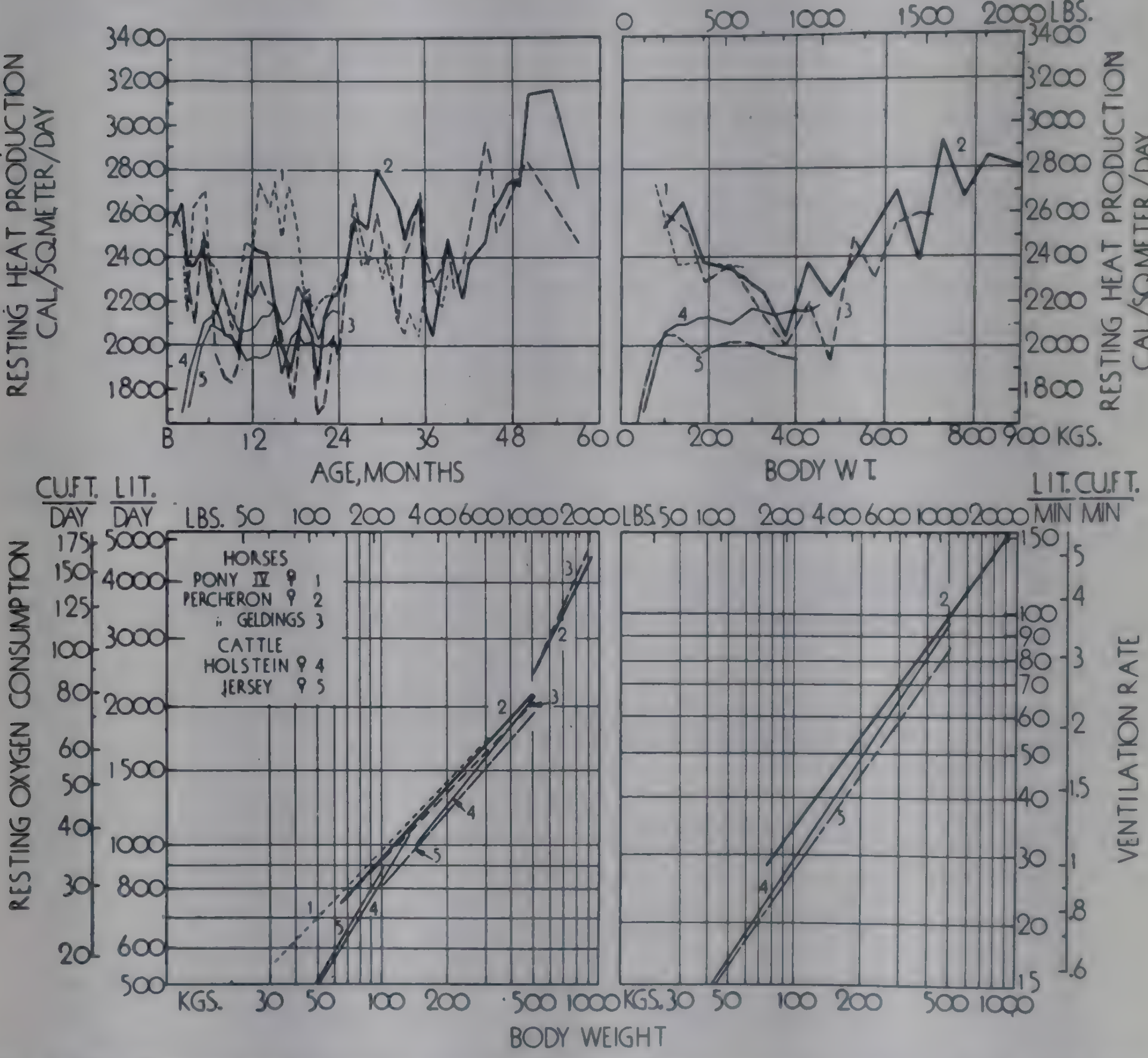

Fig. 14.11. Comparison of resting metabolism and pulmonary ventilation in horses and cattle.

The data on the Shetland ponies, Fig. 14.12, are too few to indicate the presence of breaks, if any, in the curve. The slope of the general trend, 0.52 to 0.59, is relatively low (in cattle the slopes were about 0.8 before six months and 0.6 after six months).

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[16] Benedict, F. G., "Vital Energetics," Carnegie Inst. Washington Pub. 503, 1938. Ritzman, E. G., Washburn, L. E., and Benedict, F. G., "The basal metabolism of the goat," New Hampshire Agr. Exp. Sta. Tech. Bull. 66, 1936.

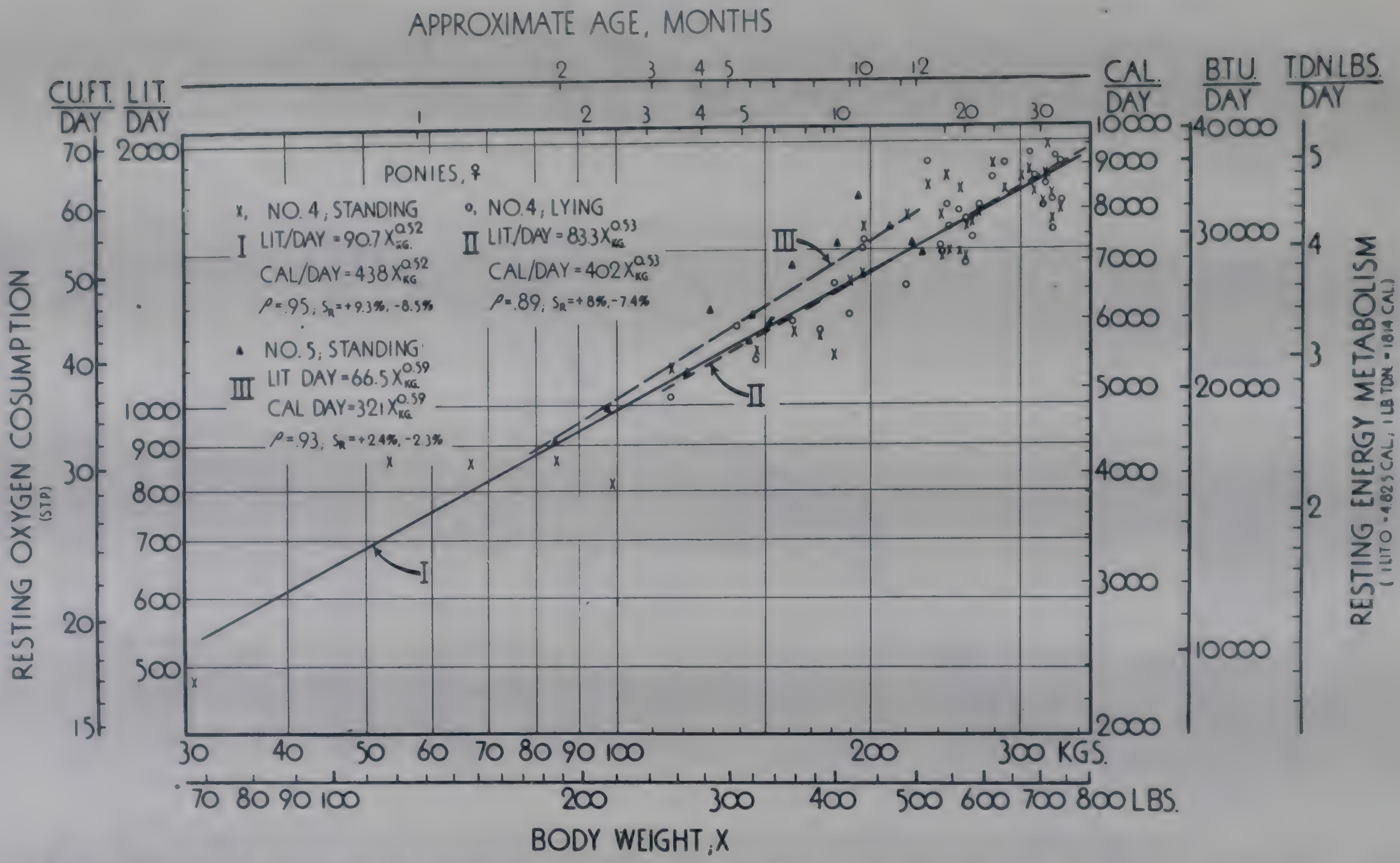

Fig. 14.12. Resting metabolism of ponies as function of body weight on logarithmic paper. Left axis oxygen consumption; right axis oxygen equivalents in Calories, Btu and TDN per day. The upper axes represent approximate ages in months.

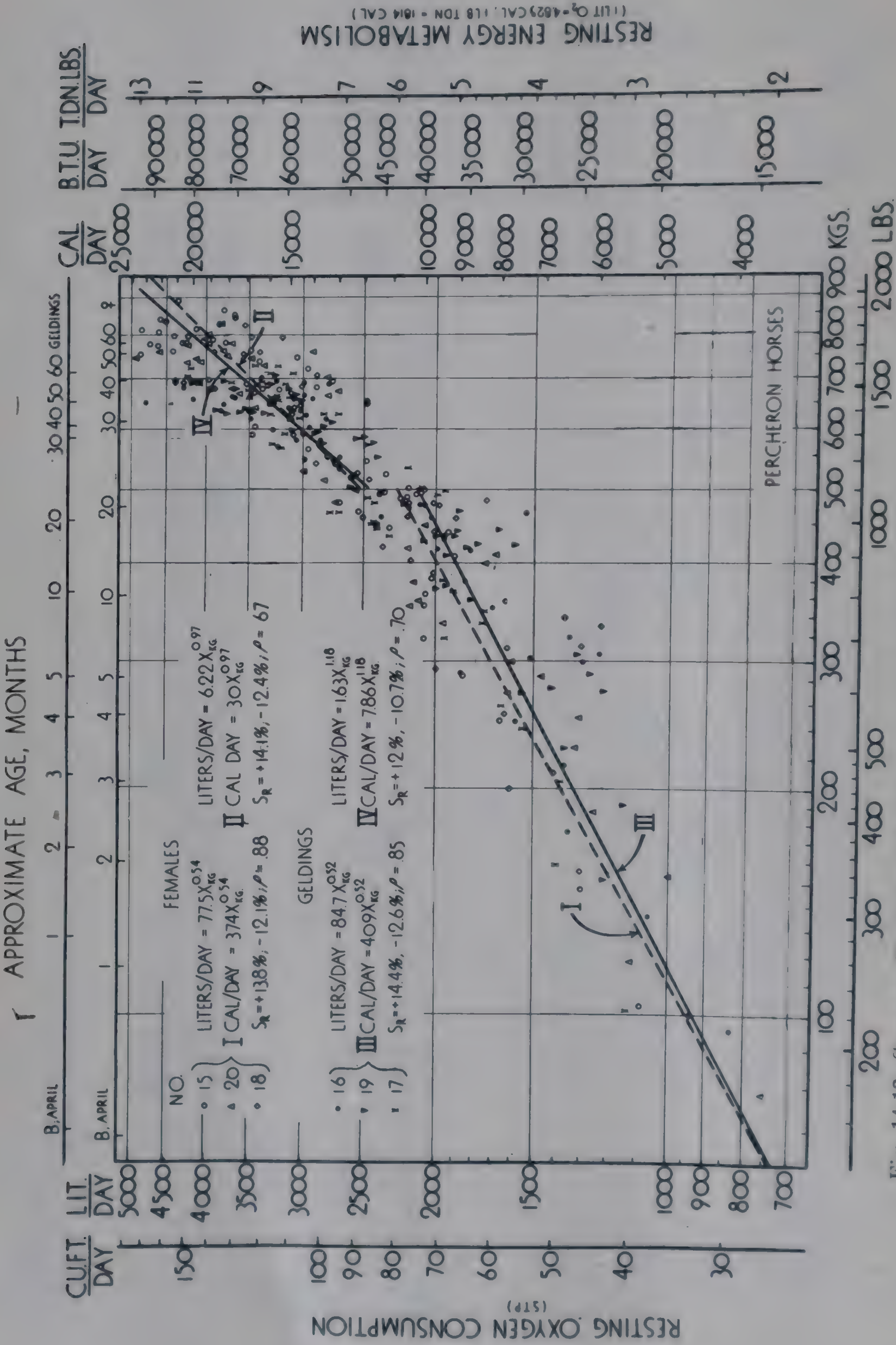

Fig. 14.13. Same as Fig. 14.12 but for Percheron horses and carried to more advanced ages.

Note especially in Fig. 14.12 that the metabolism in horses while standing is the same as while lying. Cattle, sheep, and men, on the other hand, expend about 10 per cent more energy standing than lying (Ch. 24). This observation that (unlike cattle, sheep, and men) horses have no extra energy expense for standing is not surprising since, unlike cattle, horses are equipped with very powerful suspensory and check ligaments which enable them to rest as comfortably in a standing as in a lying position. Indeed, horses usually sleep while standing. Winchester[17] measured the relative oxygen consumption of these two ponies in standing and lying positions (independently of the measurements represented in Fig. 14.12), confirming the results in Fig. 14.12.

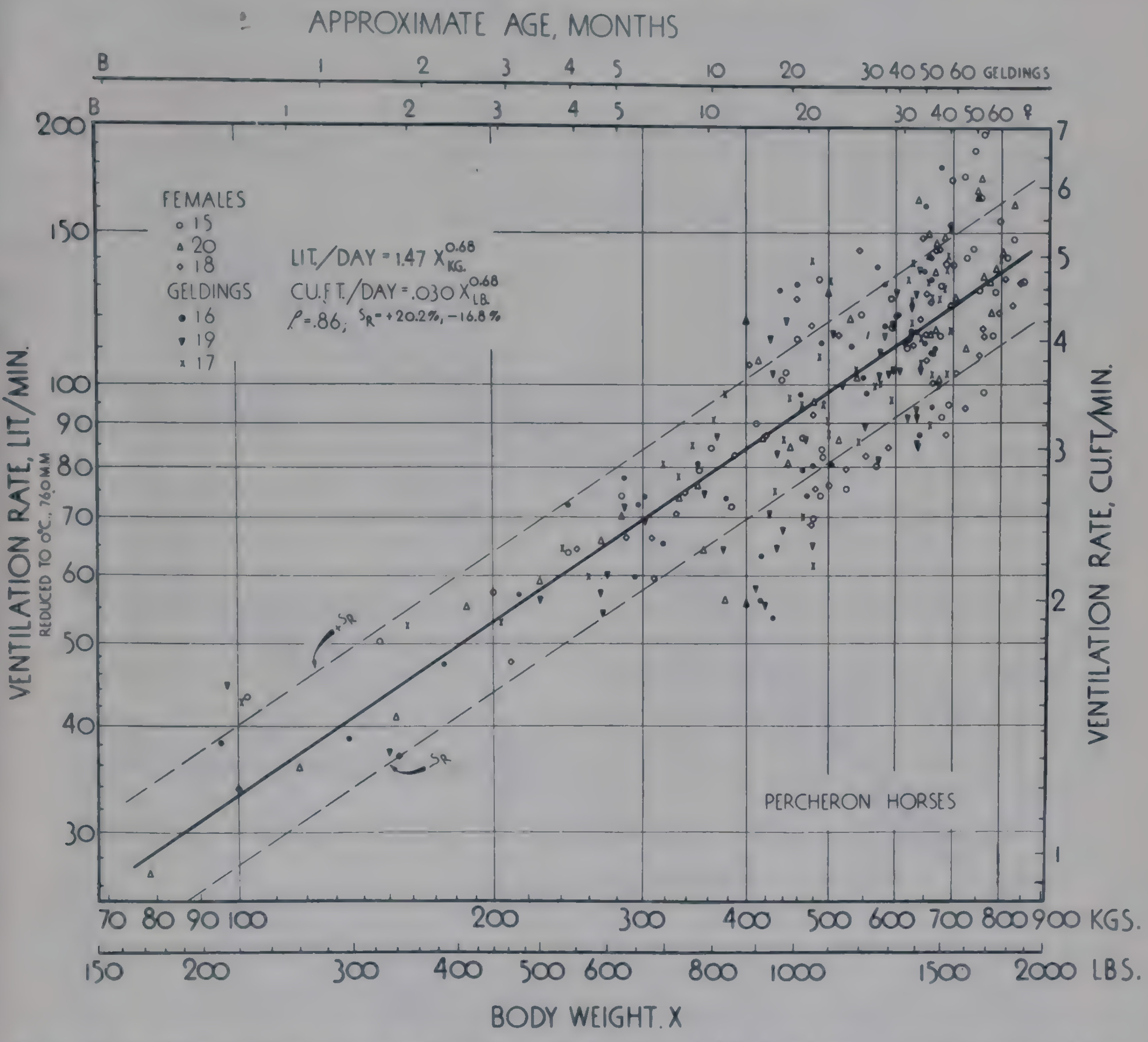

Fig. 14.14. Ventilation rate as function of body weight (and age, upper axis) of the Percheron horses.

Fig. 14.13 for the (large) Percheron horses shows a sharp change in slope, from 0.5 to 1.0, at an age of approximately two years (the pony data extend to only two years, while the Percheron data extend to 5 years). This rise is independent of sex, since castrated animals (geldings) exhibit the same rise as normal females. This slope difference is probably due to ever-increasing physical exertion. These animals were hard-working farm horses. (It is generally known that the basal or resting metabolism of active athletes is higher than of sedentary individuals of the same weight.) Not all the horses worked equally hard, or were equally muscular, which explains the rather wide scattering of the data.

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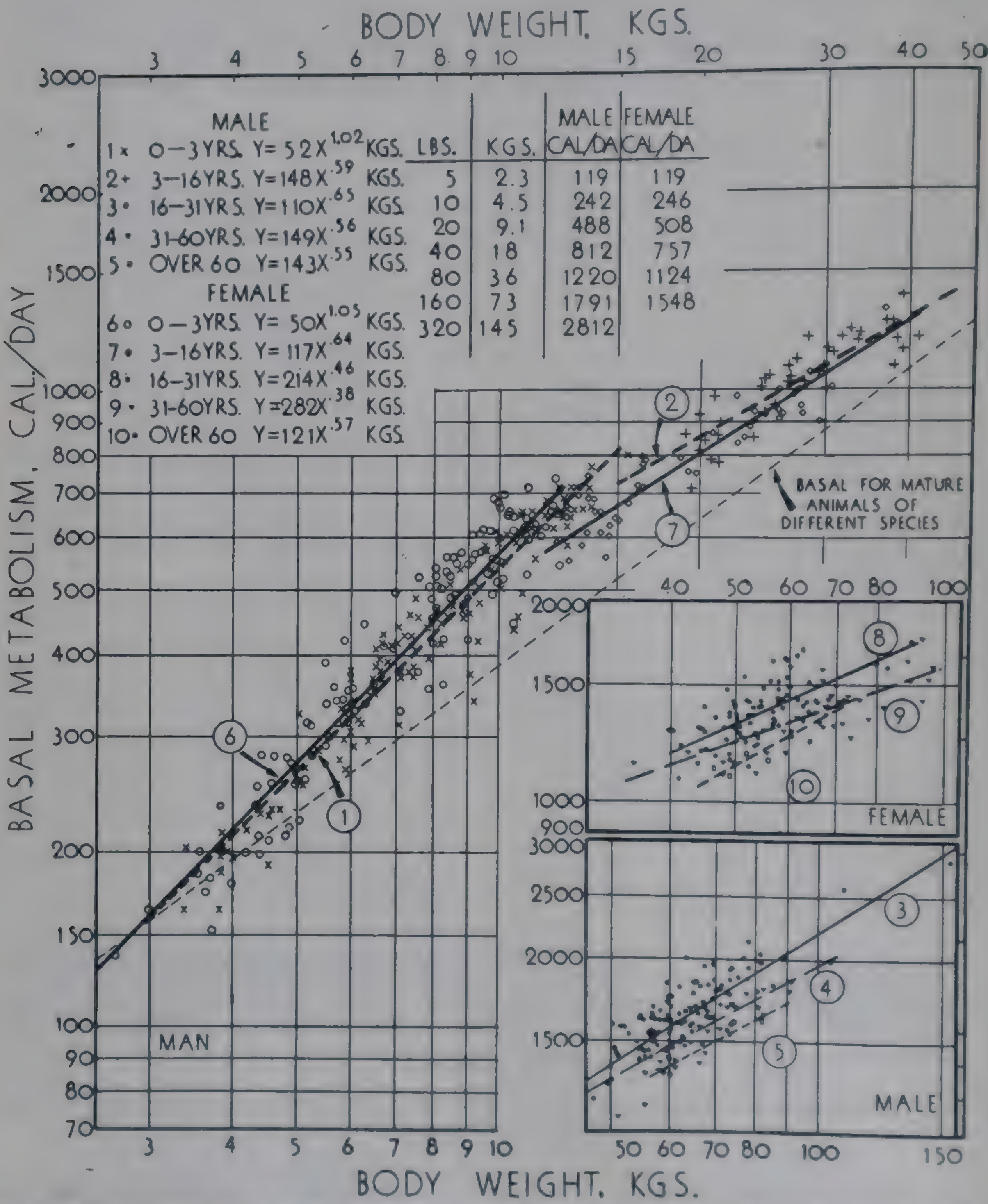
[17] Winchester, C. F., "The energy cost of standing in horses," *Science*, **97**, 24 (1943).



LBS.	KGS.	MALE CAL/DA	FEMALE CAL/DA
5	2.3	119	119
10	4.5	242	246
20	9.1	488	508
40	18	812	757
80	36	1220	1124
160	73	1791	1548
320	145	2812	

Fig. 14.15. Metabolism of children as function of body weight on logarithmic grid. For sources of data and further details see Fig. 14.16a and b.

The distribution and slope of the ventilation data for the horses, Fig. 14.14, is similar to those for cattle (Figs. 14.8 and 14.9).

As previously noted, Fig. 14.11 is a comparison of the horse and cattle data. Instead of rising, as for cattle, the metabolism per unit area declines in horses during the first few months, perhaps because of the greater restlessness of the young colts. Better data are likely to show a rise in metabolism per unit area as in cattle. For given weights horses have a higher metabolism than cattle.

The numerical data for horses are summarized in Table 14.4.

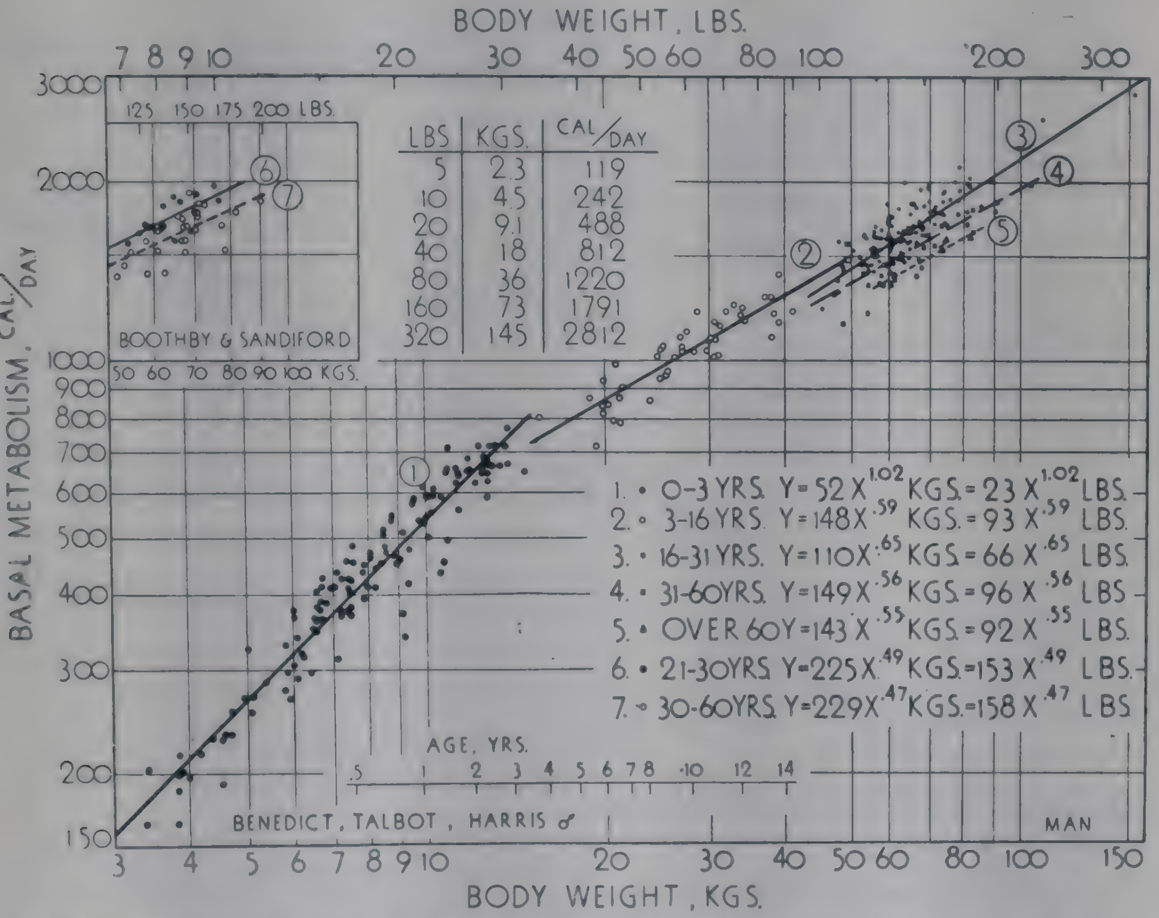


Fig. 14.16a. The same data as in Fig. 14.15 but plotted separately for males (a) and females (b), and the metabolism for various levels given for convenient comparison.

14.6: Metabolism in man. We shall not discuss the age changes in metabolism per unit area in man since this is discussed in detail in Du Bois' book and in less detail in physiology textbooks. Our remarks are confined to metabolism of the growing man of average build as a function of weight when plotted on a logarithmic grid, illustrated in Fig. 14.15, which brings out the following features.

(1) There is a change in slope in the metabolism-weight curve at approximately three years of age ("natural weaning" age?), corresponding apparently to the break at three weeks (weaning age) in rats and five months (weaning age) in cattle. This "break" corresponds to maximal metabolism per unit area (see the Du Bois insert in Fig. 14.4a).

(2) From birth to three years, the metabolism varies directly with body weight; the slope of the curve is 1.0. Extrapolating the equation to intra-uterine growth gives zero metabolism at zero weight, indicating the possibility that this postnatal metabolism equation also represents prenatal metabolism. While, as previously explained, it would be impossible for the metabolism *per unit surface area* to be the same in early prenatal as during postnatal life, the metabolism could well be the same *per unit weight*, 50 Cal/kg/day, as indicated by the equation $Y = 50X^{1.05}$ (Fig. 14.15). There is no significant sex difference in metabolism before three years.

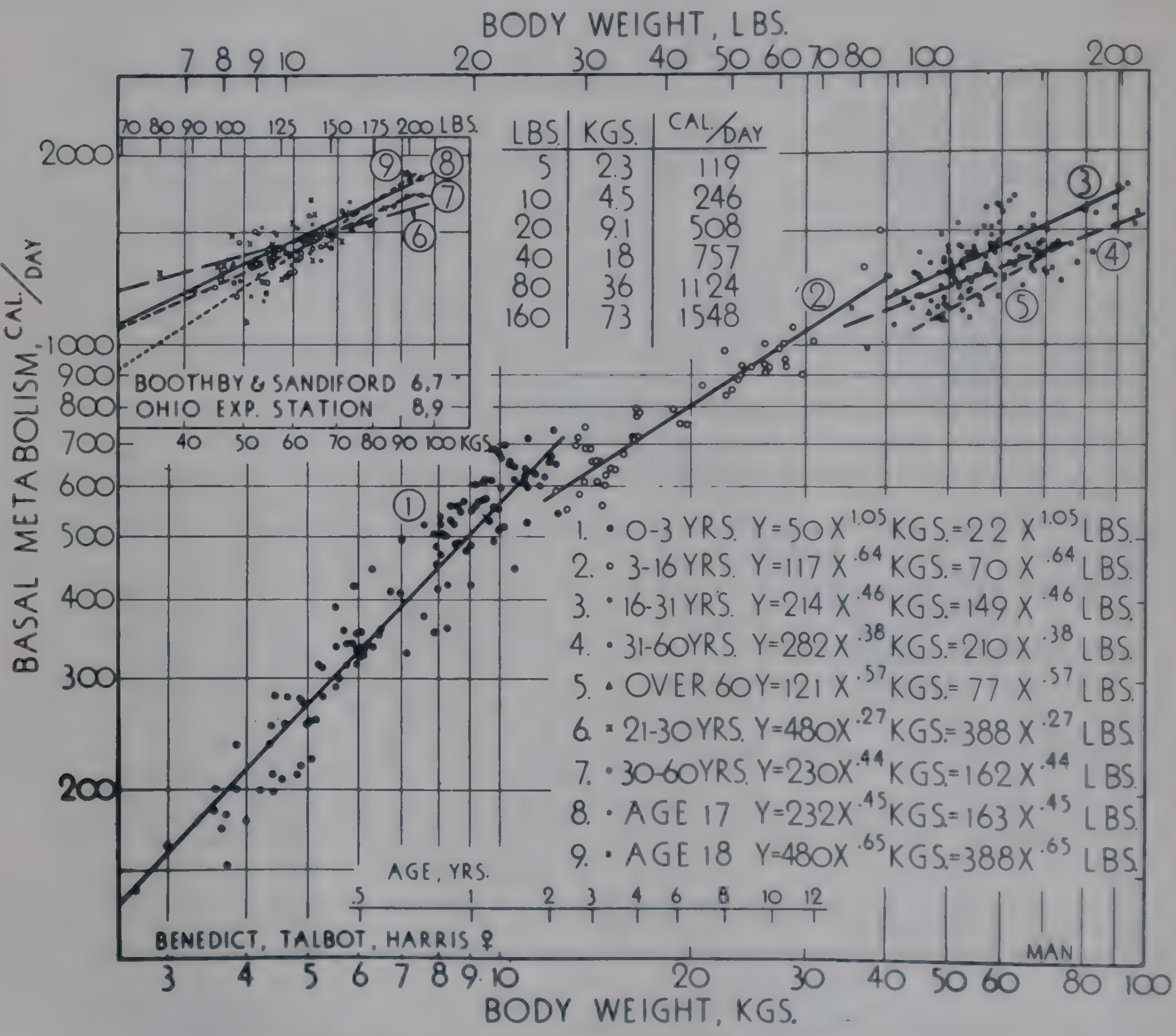


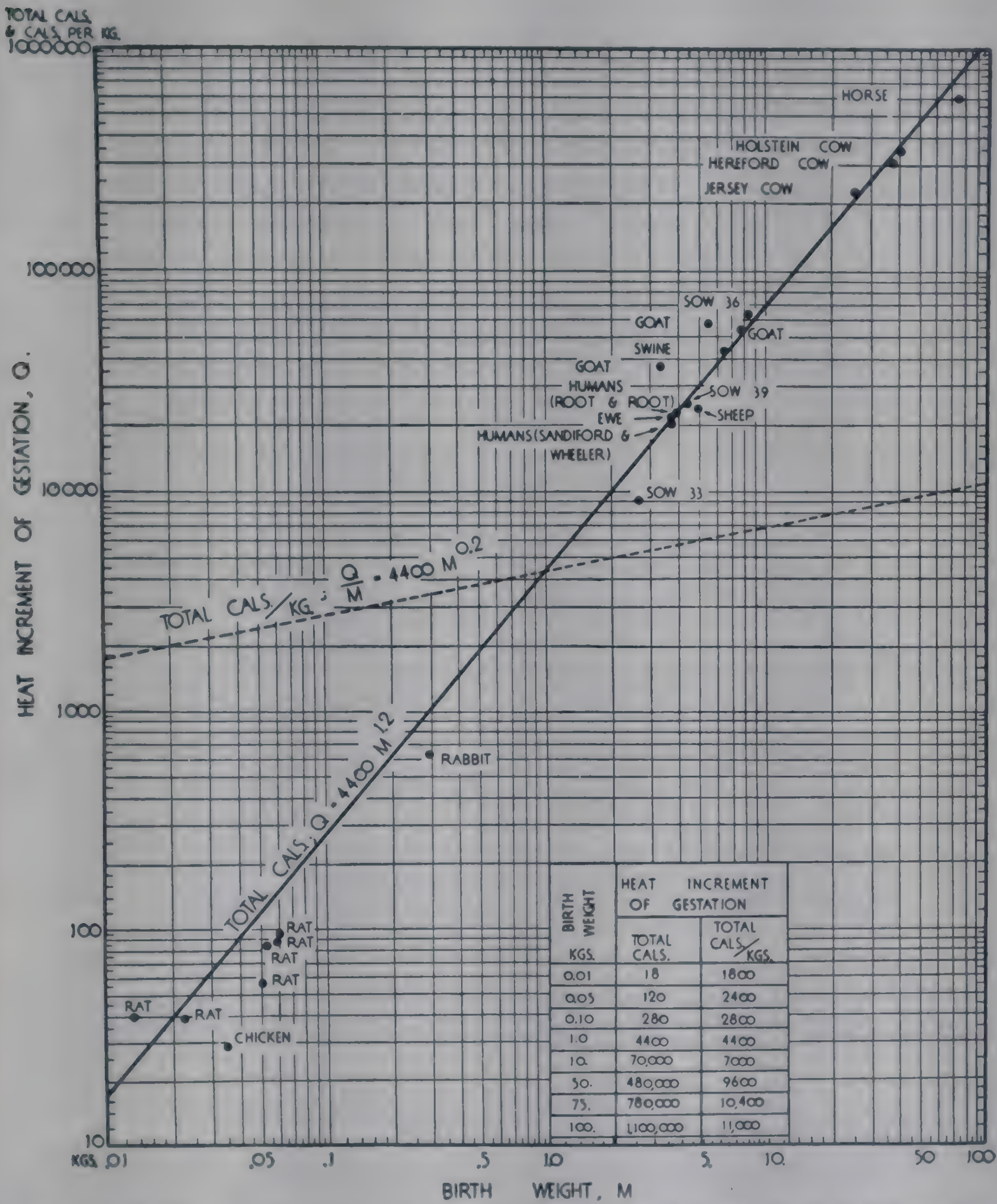
Fig. 14.16b. See legend of Fig. 14.16a.

(3) Between the ages of 3 and 16 years the slope of the curve is not 1.0, as it was before 3 years, but about 0.6 (near the value for cattle, goats, and horses previously discussed). The slope is 0.59 for boys and 0.64 for girls, and boys tend to have the higher metabolism.

(4) Between 16 and 31 years, the slope tends to be higher for men than for women, 0.65 for men and 0.46 for women.

(5) Sex differences disappear after 60 years.

The light, broken curve in Fig. 14.15 represents the metabolism of mature animals of different species (Fig. 13.7). On maturing, the metabolism of man approaches that of the general curve relating metabolism to weight in mature animals of other species.



BIRTH WEIGHT KGS.	HEAT INCREMENT OF GESTATION	
	TOTAL CALS.	TOTAL CALS./KGS.
0.01	18	1800
0.05	120	2400
0.10	280	2800
1.0	4400	4400
10.	70,000	7000
50.	480,000	9600
75.	780,000	10,400
100.	1,100,000	11,000

Fig. 14.17. The relation between the heat increment of gestation, Q, and birth weight, M, plotted on a logarithmic grid. The broken curve and solid circles represent the ratios of the heat increments of gestation, to birth weight of young; the continuous heavy curve and crosses represent the total heat increment of gestation plotted against birth weight.

Figs. 14.16a and b represent the same data as Fig. 14.15, but show how the metabolic level tends to drop for given body weights at successive age intervals (#3, 16 to 30 years; #4, 30 to 60 years; #5 over 60 years). Other aspects of metabolism during aging, especially the oxygen consumption per pulse per unit weight, are discussed in Chapter 18.

Some may prefer the results in numerical form given in Table 14.5. This table shows the total metabolism in Cal/day and also per kg, per lb, and per sq meter for various age intervals and body weights. The metabolism energy is here also expressed in terms of milk energy. Thus, a 14-kg or 31-lb infant expends as much energy for resting maintenance per 24 hours as is given off on burning in a bomb calorimeter approximately a quart, or liter, of milk containing 4 per cent fat. This does not mean that a quart of milk is all the energy that a 14-kg infant needs, since there is a variable energy expense in utilization of the milk and the infant also needs food for growth and for various activities above that of resting maintenance.

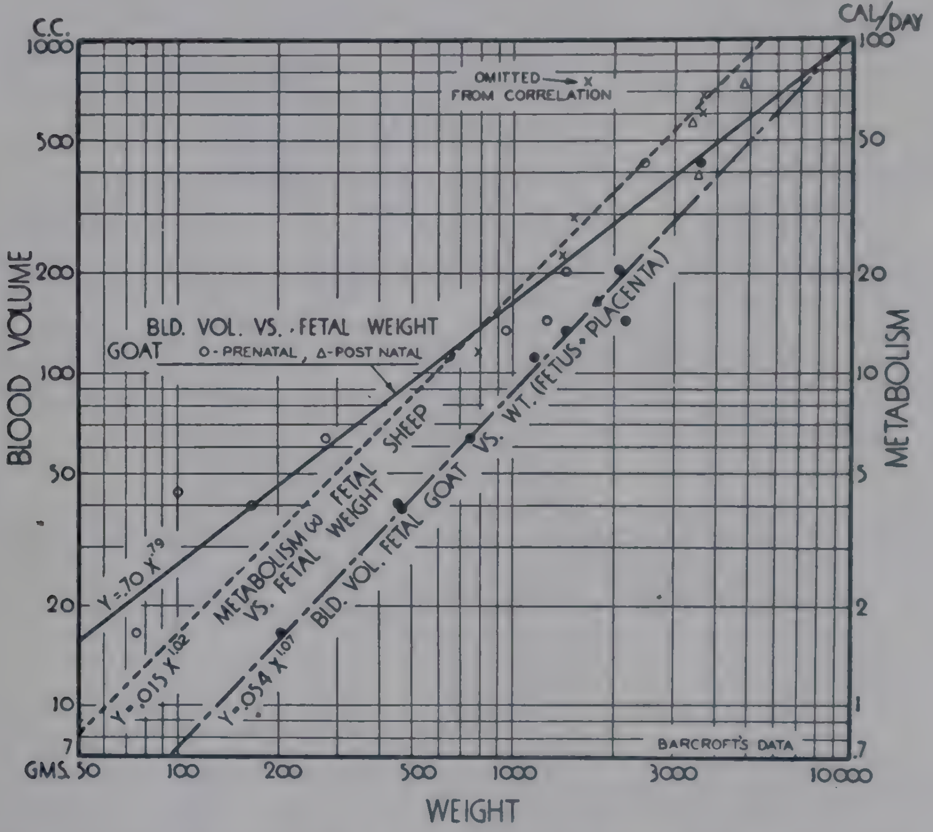


Fig. 14.18. Metabolism as function of fetal weight of sheep on a logarithmic grid; also blood volume as function of fetal weight and fetal plus placental weight.

14.7: Prenatal heat production in relation to birth weight. We measured[18] the heat increment of gestation (the extra heat production of resting animals during gestation above the non-gestating level) of rats, cattle, horses, sheep, and swine. As it was unfortunately necessary to confine the measurements to young primapara, the heat and weight increments of gestation were complicated by the growth of the mother. It may nevertheless be instructive to correlate the heat increment of gestation with the birth weight of the young.

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[18] Brody, S., Mo. Agr. Exp. Sta. Res. Bull. 283, 1938.

This heat increment of gestation, of course, includes not only the total of the "basal" or "resting" metabolism of the embryo and fetus from conception to birth but also that of the involved accessory structures and of the maternal body, whose heat production is accelerated during gestation by increased endocrine activity.

The result of the correlation between the heat increment of gestation and birth weight is shown in Fig. 14.17 (plotted from Table 14.6) and is given by the equation $Q = 4400M^{1.2}$ in which Q is the total heat increment in Calories and M is birth weight in kilograms. The heat increment of the incubating chick is included in the chart, but not in fitting the equation to the data.

This equation means that the production of a 1-kg young is associated with a heat increment of gestation of 4400 Cal. The heat increment per kg young necessarily varies with the time required to develop it. This is probably the meaning of the exponent 1.2: increasing the birth weight 100 per cent (and therefore increasing the time of prenatal growth) tends to be associated with an increase in heat production of 120 per cent. The longer the prenatal growth period, the greater the prenatal maintenance cost per unit young, and also for the accessories and mother's heat increment of gestation. Yet the data on slow-growing man (by Root and Root and by Sandiford and Wheeler) fall right on the line. Rabbit and most rat data, however, fall below the line.

The regularity of distribution of the data in Fig. 14.17 tempts one to say that the given equation represents a "law" of constant gestation energy analogous to Rubner's "law" of constant growth energy (Ch. 3), which states that the construction cost of body substance during the first prenatal doubling of body weight is 4800 Calories per kilo (except for man). While the two constants, 4400 Calories in Fig. 14.17 and 4800 of Rubner, appear similar, they evidently reflect different situations: Rubner's value refers to the energy cost of postnatal growth of the individual, including the stored energy, whereas the 4400-Cal value in Fig. 14.17 refers to the heat increment of gestation, including the heat increments of all accessory structures and of the mother, but not including the stored energy. Moreover, Rubner's "law" assumes a linear relation (the exponent is 1.0) whereas the equation in Fig. 14.17 indicates an exponent of 1.2.

The gestation heat increment thus includes (1) the energy expense of maintenance of the pregnant uterus; (2) "work" of growth; (3) increased work of the maternal organism (increased circulatory, respiratory and excretory activities); (4) endocrine influences on metabolism of the mother. Even in the incubating chick there may be an extra heat production by the allantois, yolk sack, and even an extra heat production associated with the presence of the yolk[19]; and the situation is still more complex in mammals. The problem of prenatal growth has been adequately discussed by Needham[6]. The following notes review briefly the literature as it bears particularly on the above discussions.

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[19] Barott, H. G., Byerly, T. C., and Pringle, E. M., "Effect of removal of unabsorbed yolk on heat production of chicks," *J. Nut.*, **11**, 191 (1936). Barott, "Effect of temperature and other factors on energy metabolism of chick embryos," U. S. Dept. Agr. Tech. Bull. 553, 1937.

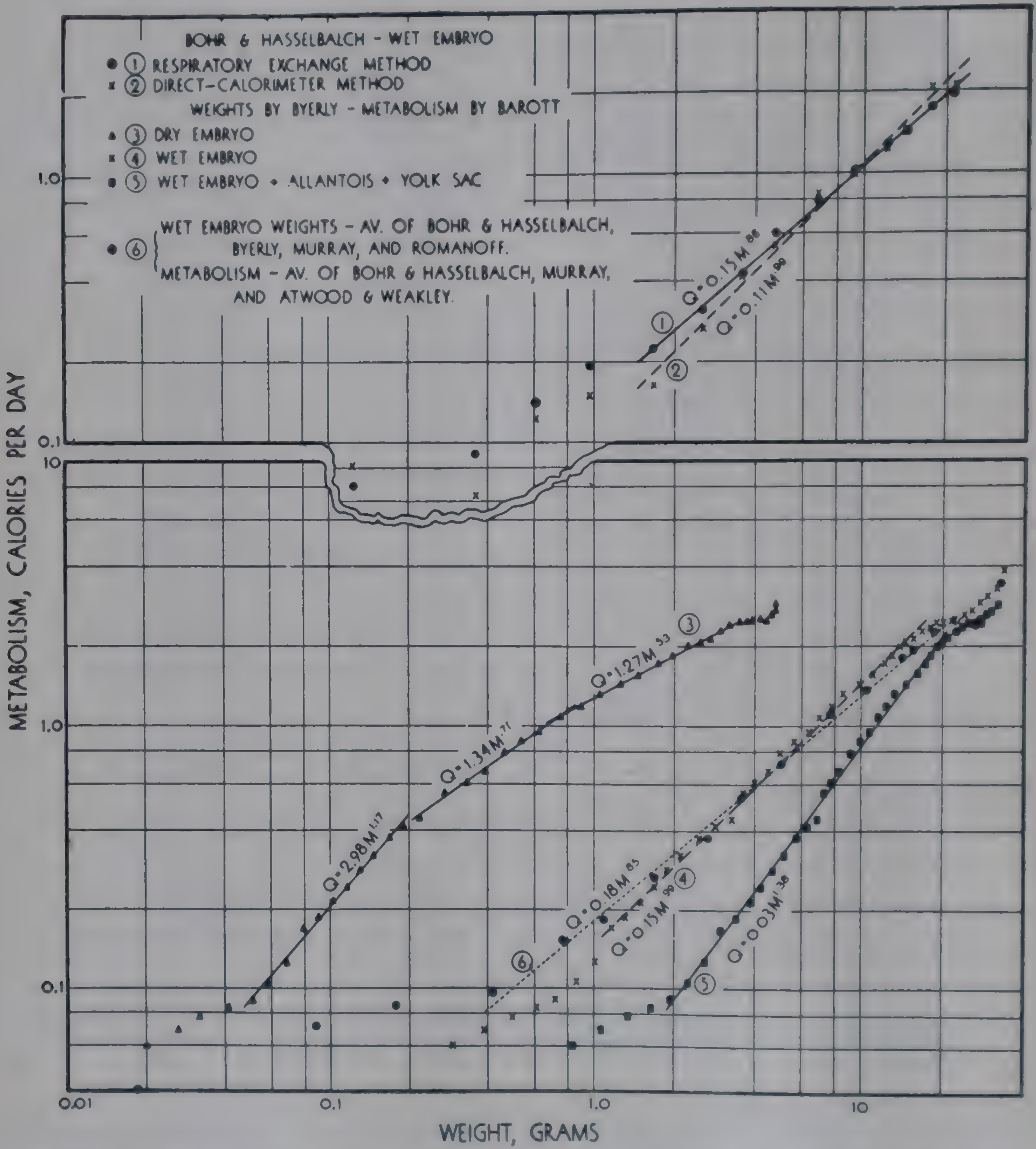

Fig. 14.19. The metabolism of the chick embryo as function of body weight on a logarithmic grid.

According to Barcroft[20], the embryo is under no necessity to maintain its own body temperature; it has no surface, if the word "surface" be used in the physiological sense, as an area from which heat is dissipated. There seems little point, therefore, in calculating the relation of heat production or blood volume to the cutaneous area. The blood volume is more reasonably represented as a percentage of weight of the actual embryo or as a percentage of the embryo plus the placenta, through which circulation takes place, and which may therefore be regarded as an integral part of the fetus.

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[20] Barcroft, J., *Physiol. Rev.*, **16**, 103 (1936).

Barcroft measured the oxygen consumption and blood volume of the fetal sheep and goat. We have computed the power function relating oxygen consumption and blood volume to body weight with the result shown in Fig. 14.18. The fetal oxygen consumption is seen to increase directly with simple body weight ($W^{1.0}$). The equation given in Fig. 14.18 is

$$Y = 0.015X_g^{1.0}$$

meaning that the heat production per unit weight is approximately constant, 0.015 Cal/g/day or 15 Cal/kg/day, a comparatively low value, numerically equal to the basal metabolism per kilo per day of mature cattle or horses. (The metabolism per square meter as computed by us is between 200 and 600 Cal per day.) The blood volume in the fetal goat increases with the 0.79 power of fetal weight and with the 1.0 power of the combined weight of the fetus and placenta. These results substantiate our suggestion that early metabolism varies not with surface area but with simple weight, and contradict Rubner's assumption that it varies with surface area.

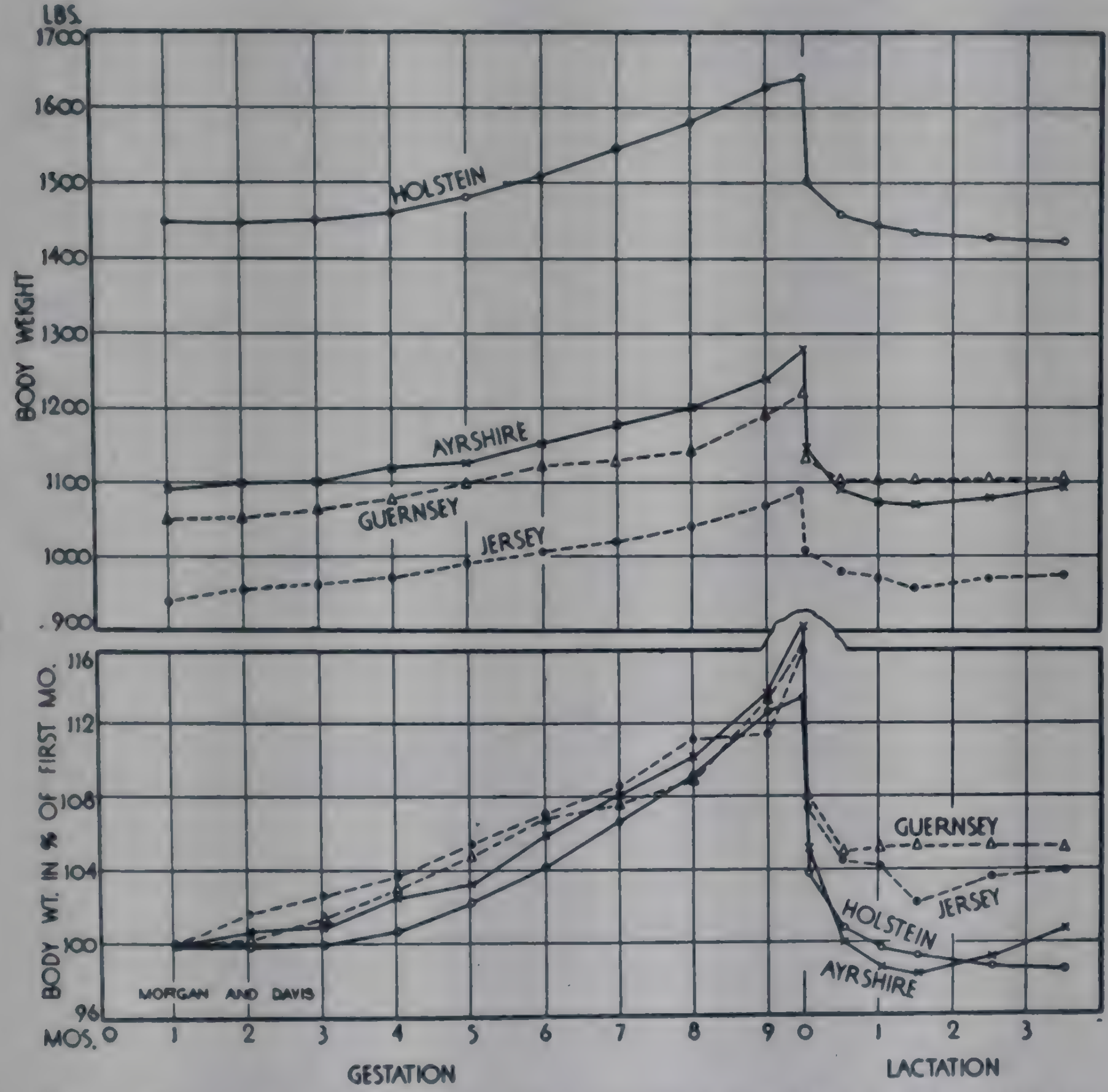

Fig. 14.20a. Changing body weight with advancing gestation and lactation in dairy cattle. Plotted by us from data by R. F. Morgan and H. P. Davis, Univ. Neb. Agr. Exp. Sta. Res. Bull. 82, 1936.

The metabolism of the chick embryo also varies more nearly with simple weight ($W^{1.0}$) than with surface area. This is shown in Fig. 14.19, plotted from the indicated sources. By weight we mean wet weight. When metabolism is plotted against dry weight (curve 3, Fig. 14.19), the slope ranges from 1.2 to 0.53, depending on the developmental stage.

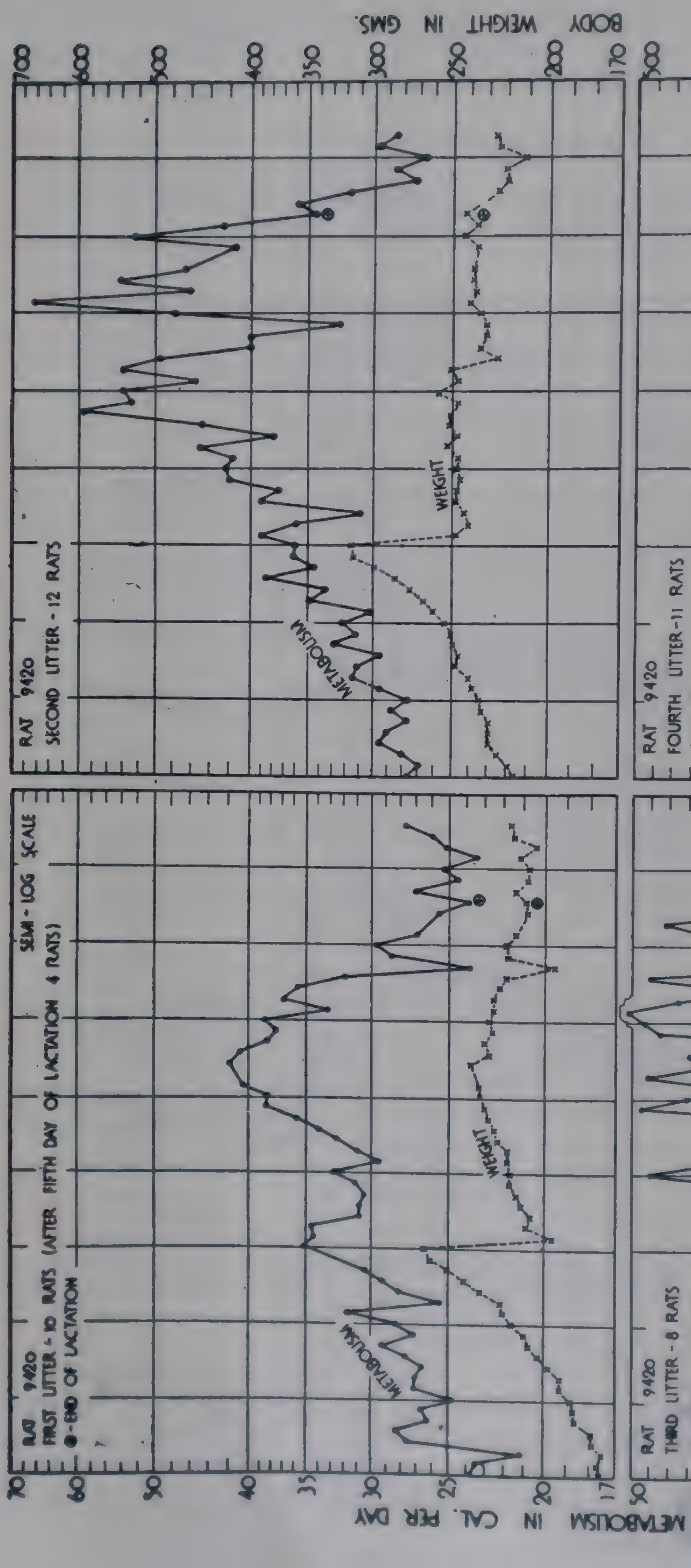

Fig. 14.20b. Changing body weight (right axis) and metabolism (left axis) with advancing gestation and lactation in the rat during first, second, third, and fourth pregnancies.

Several other references may be cited. Murlin[21] reported on the pregnancy metabolism of a dog. Her heat production during sex rest was 505 Cal; 3 days before giving birth to 1 puppy, 551 Cal; 3 days before giving birth to 5 puppies, 765 Cal. In other words, the gestation metabolism above sex rest was 46 Cal for 1 puppy, and about 5 times (5.6 times) that much, 260 Cal, for 5 puppies. Pommerenke, Haney and Meek[22] investigated the energy metabolism of gestation and lactation in rabbits which confirm Murlin's results on the dog.

Carpenter and Murlin[23] reported that the maternal organism and fetus function as two separate units in their energy consumption; because the metabolism of a pregnant mother shortly before paturition was nearly the same as mother *and* child after childbirth. Sandiford and Wheeler[24] came to a similar conclusion, but on the basis of surface-area computations which were criticized by Rowe and Boyd[25].

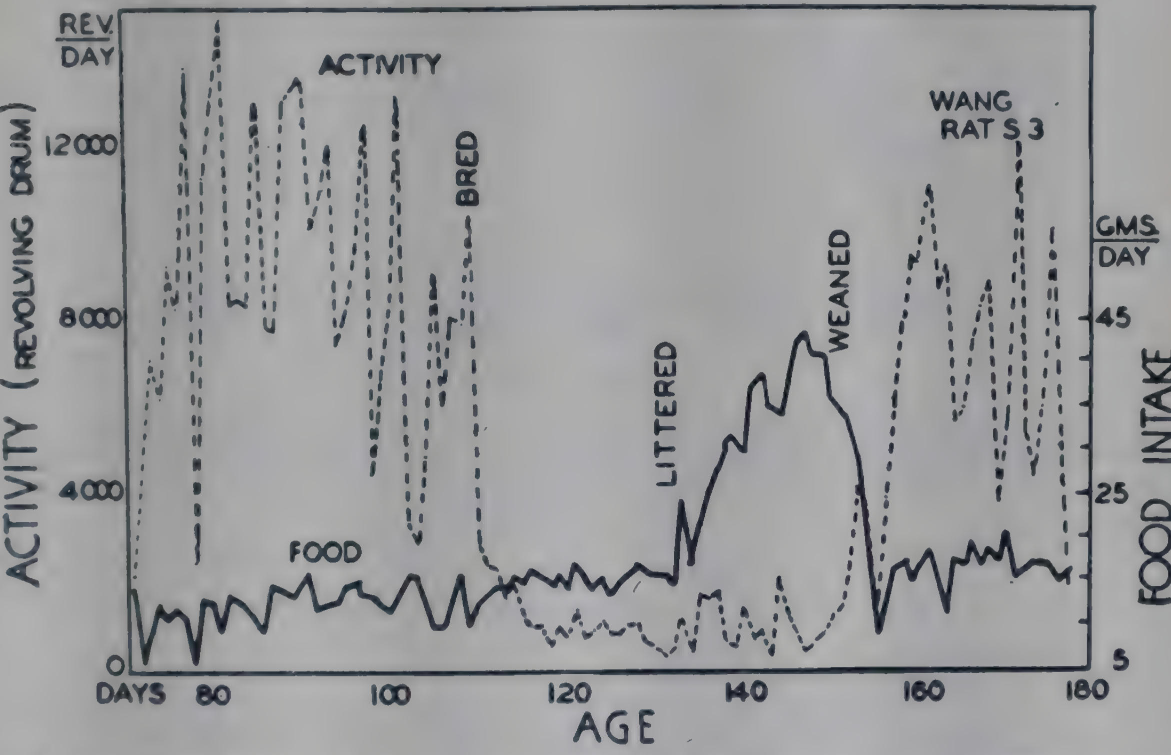

Fig. 14.20c. The course of changing activity and food intake with advancing gestation and lactation in the rat. From Ging H. Wang, *Am. J. Physiol.*, 1925, p. 736.

Schwarz and Drabkin[26], and others, attributed increased heat production during gestation to increased thyroid activity. This conclusion is based in part on the rise in blood iodine from the second (15.5 gamma per cent) to the tenth lunar month (22.5 gamma per cent) and its decrease during the first two weeks of puerperium; in part on the hypertrophy of the anterior pituitary, which presumably increases in its thyrotropic activity during pregnancy; and in part on hypertrophy of the thyroid during pregnancy.

Root[27] reported data on basal metabolism of a primipara in whom pregnancy was uncomplicated by gain in adipose tissue or disease. The basal metabolic rate during the fourth month was essentially that predicted by the standard for non-pregnant women of the same age, height and weight, then followed by a steady increase until eleven days before delivery, when the total basal metabolism was 23 per cent above that during the fourth month—an increase out of proportion to the standard prediction tables for normal women, with corresponding gain in weight. The Cal/kg gain in basal metabolism from the fourth month of pregnancy to the eleventh day before delivery was 7.6 per cent. Following delivery, although the subject's weight remained nearly stationary, the basal

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[21] Murlin, J. R., *Am. J. Physiol.*, **23**, 32 (1908–9).

[22] Pommerenke, W. T., Haney, H. F., and Meek, W. J., *Am. J. Physiol.*, **93**, 249 (1930).

[23] Carpenter, T. M., and Murlin, J. R., *Arch. Int. Med.*, **7**, 184 (1911).

[24] Sandiford, I., Wheeler, T., and Boothby, W. M., *J. Biol. Chem.*, **62**, 329 (1924); *Am. J. Physiol.*, **96**, 191 (1931).

[25] Rowe, A. W., *et al.*, *J. Nut.*, **5**, 551 (1932), **7**, 591 (1934); *Am. J. Physiol.*, **71**, 667 (1925).

[26] Schwarz, O. H., and Drabkin, C., *Am. J. Obst. and Gyn.*, **22**, 3 (1931).

[27] Root, H. F., and Root, H. K., *Arch. Int. Med.*, **32**, 411 (1923).

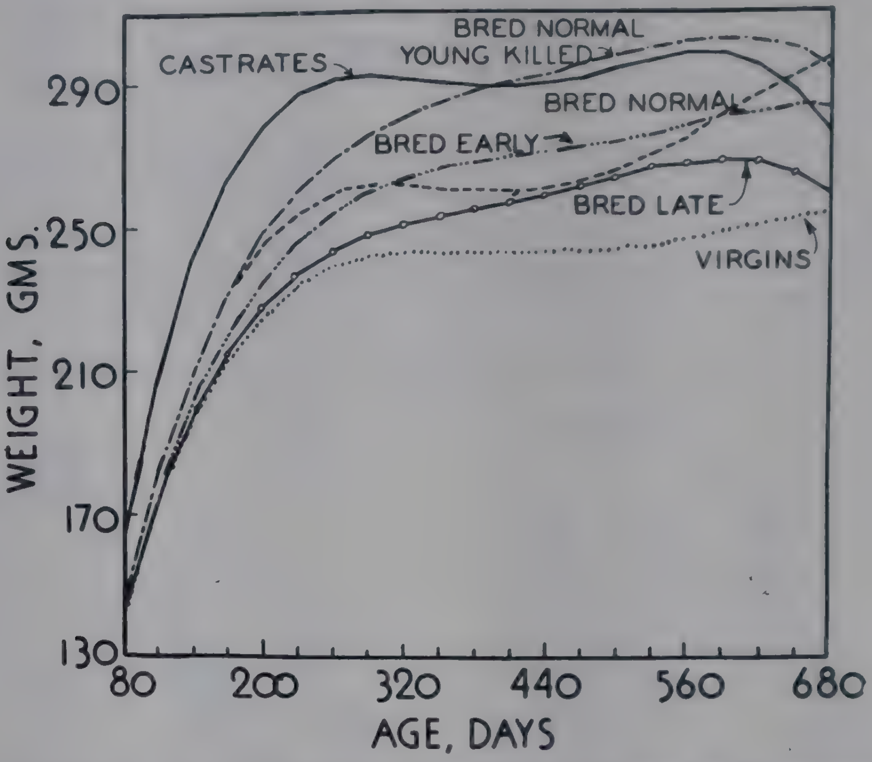

Fig. 14.21a. Influence of reproductive condition on growth and reproduction of white rats. From R. Bogart, G. Sperling, L. L. Barnes, and S. A. Asdell, *Am. J. Physiol.*, **124,** p. 362 (1940) and from Asdell, Bogart and Sperling, Cornell Univ. Memoir 238, 1941, p. 6.

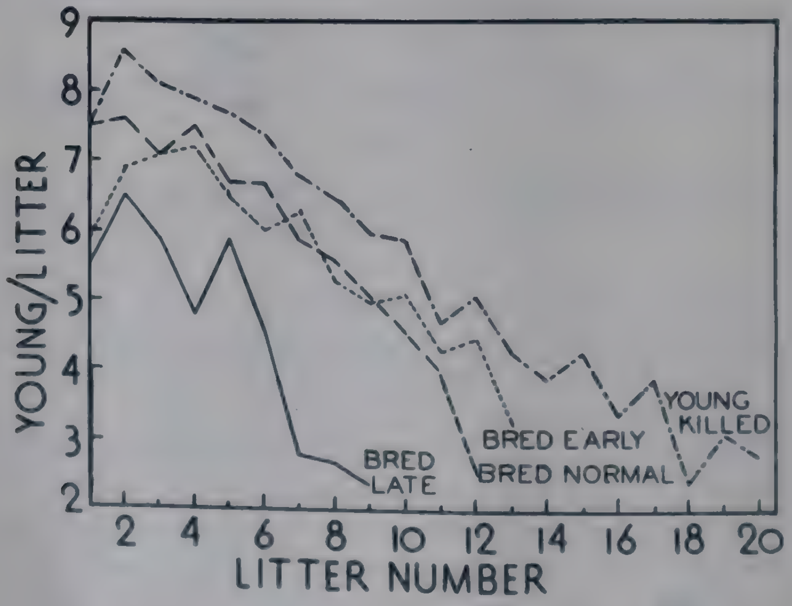

Fig. 14.21b. See legend of Fig. 14.21a.

metabolism fell to 9.6 per cent below the rate observed during the fourth month of pregnancy. "The high metabolic rate during the last month of pregnancy only partially reflects the much higher metabolic rate of the fetus per unit of weight, since the maternal weight is made up in part of inactive tissues such as edema and the fluid contained in the amnion. It appears that the metabolism of the fetus at term was approximately 37 Cal/kg, whereas the basal metabolism of the mother was 23.5 Cal/kg during the fourth month of pregnancy and 22.1 Cal/kg one month after delivery".

A report[28] on basal energy and mineral metabolism on a young primipara for 66 days ante-partum concludes thus: "The rise in metabolism throughout the latter part of pregnancy parallels the cumulative nitrogen and sulphur curves. It is felt that a hormone influence responsible for the synthesis of the new mass of protoplasm must likewise be included in any explanation of the phenomenon".

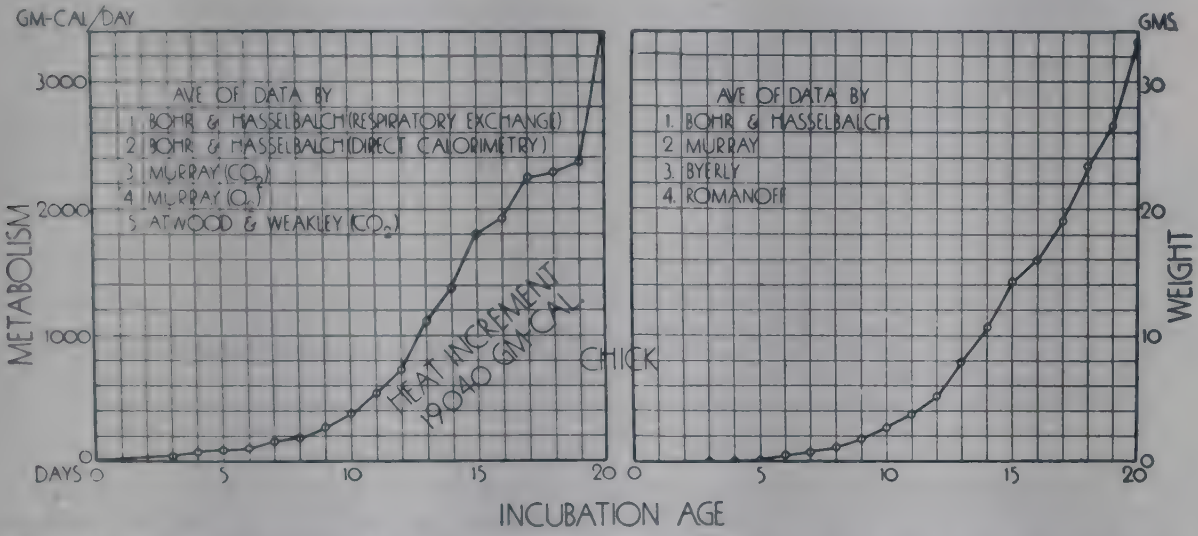

Fig. 14.22a. Age course of growth in weight (right) and of heat production (left) of the chick. The area under the curve is the total heat production, or heat increment of incubation, is seen to be 19.04 Cal.

Several reports point to a decline in metabolism in the early stages of pregnancy[29], perhaps due to decline in muscular activity. Data on rats by Wang[30] show a drop in activity from 16352 drum revolutions (in an exercising cage) preceding conception to 2779 revolutions following conception. Slonaker's[31] data show a similar decline: "I have found that both during gestation and pseudopregnancy there is great reduction in activity accompanied by little change in food consumption. The energy which is usually used for activity is then used for growth".

While the weight gains during pregnancy are considerable (Fig. 14.20 to 14.23), the food consumption is not increased proportionately because the energy saved by decreased muscular activity during pregnancy is used for the growth. Wang quotes Schick's observation that humans instinctively refrain from bodily activity during pregnancy, and this energy saving is used for meeting the increased demand for nourishment. Data by Macy and co-workers[32] on food consumption of human mothers demonstrate this fact. Eckles[33] reported that pregnancy in dairy cattle, leading to a 16 per cent increase in body weight (Fig. 14.20a), does not involve an increase in feed consumption. The 16 per cent weight increase during pregnancy includes relatively

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[28] Johnston, J. A., Macy, I. G., *et al.*, *J. Nut.*, **15**, 513 (1938).

[29] For man, see Rowe and Boyd, *J. Nut.*, **5**, 551 (1932). For sheep, see Ritzman and Benedict, N. H. Agr. Exp. Station Tech. Bull. 45, 1931.

[30] Wang, G. H., *Comp. Psychol. Monogr.*, **2**, No. 6 (1923), and *Am. J. Physiol.*, **71**, 736 (1935).

[31] Slonaker, J. R., *Am. J. Physiol.*, **71**, 362 (1924-5).

[32] Shukers, C. F., *et al.*, *J. Nut.*, **4**, 399 (1931). Coons, C. M., *et al.*, Okla. Agr. Exp. Sta. Bull. 223, 1935.

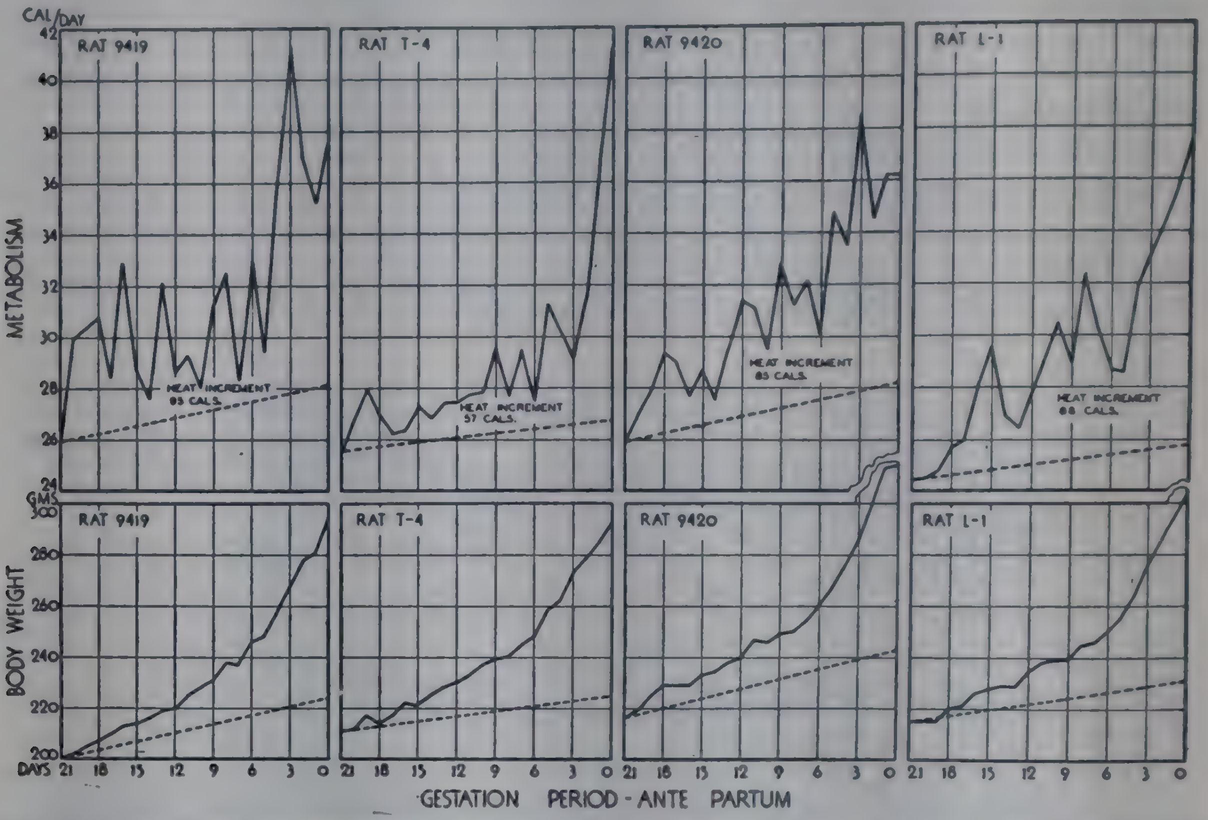

Fig. 14.22b. Heat increments of gestation of rats and horses; these are represented by the areas between the curve of heat production and the base line assumed to represent the heat production of the animals if they were not pregnant. The weight increments of gestation are likewise shown graphically.

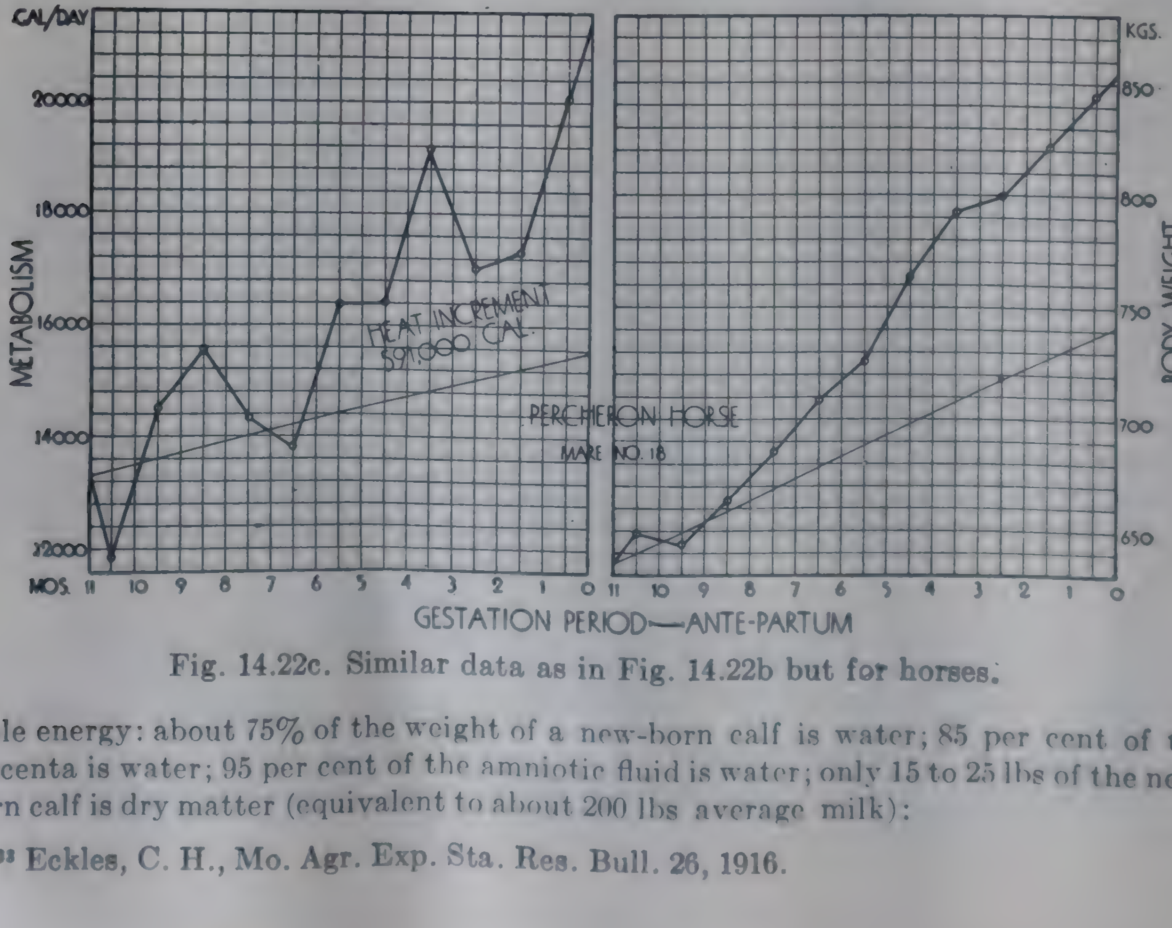

Fig. 14.22c. Similar data as in Fig. 14.22b but for horses.

little energy: about 75% of the weight of a new-born calf is water; 85 per cent of the placenta is water; 95 per cent of the amniotic fluid is water; only 15 to 25 lbs of the new-born calf is dry matter (equivalent to about 200 lbs average milk):

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[33] Eckles, C. H., Mo. Agr. Exp. Sta. Res. Bull. 26, 1916.

Calves from experimental cows

Calf (lbs)	Water (lbs)	Dry matter (lbs)	Protein (lbs)	Fat (lbs)	Ash (lbs)
75	54.8	20.2	14.2	2.5	3.2
49	35.4	13.1	9.2	1.6	2.1
95	69.4	25.6	18.0	3.2	4.0
83	60.3	22.2	15.6	2.8	3.5

Amniotic fluid and placenta

	Amniotic fluid	Placenta
Weight (lbs)	32.7	18.3
Water (%)	95.9	85.6
Fat (%)	0.92	0.92
Protein (%)	3.36	12.20
Ash (%)	0.65	0.89

Constituents produced by cow in amniotic fluid and placenta

	Amniotic fluid (lbs)	Placenta (lbs)	Total (lbs)
Water	30.7	15.4	46.1
Dry matter	1.3	2.6	3.9
Fat	0.03	0.16	0.19
Protein	1.07	2.19	3.26
Ash	0.21	0.16	0.37

While Eckles' cows made normal pregnancy gains on a maintenance ration, Cole and Hart[34] observed increased food consumption in rats by the second day after conception, and that pregnancy stimulates the appetite and growth of rats beyond that of non-bred litter-mate controls (Fig. 7.4). They postulated that pregnancy stimulates the anterior pituitary to secrete one or more hormones involved in increasing appetite. The excess gains made by the pregnant rats remain fairly constant for the first six pregnancies, after which further pregnancies have less effect. The excess gains are made, for the most part, during pregnancy, although rats suckling four to six young continue to gain as rapidly as non-bred controls.

Mumford first observed at the Missouri Experiment Station[35] that early breeding of sows does not reduce their ultimate size and that delaying breeding reduces the ultimate body size as indicated by the following summary:

Age of breeding of sows (days)	Mature weight of sows (lbs)	Total litter weight at birth
218	415	20.0
479	401	19.9
838	384	14.9

Slonaker[36] first observed this effect on rats, confirmed by Cole and Hart, and by Bogart *et al.*[37], who observed that breeding rats grow more rapidly and for a longer time than non-breeding. It is the heavy lactation that constitutes the drain on the mother not the gestation. Bogart attributes the more rapid growth of breeding rats not to the growth-stimulating effect of gestation as such, but to the removal by the corpus luteum of the growth-inhibiting effect of estrogens. This is substantiated by the growth-stimulating effect of pseudopregnancy.[38] Ovariectomy has a similar growth-stimulating effect by eliminating the growth-retarding estrogenic influences[37] (Sect. 7.2.1)

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[34] Cole, H. H., and Hart, G. H., *Am. J. Physiol.*, **125**, 589 (1938).

[35] Mo. Agr. Exp. Sta. Res. Bull. 118, 1928.

[36] Slonaker, J. R., *Am. J. Physiol.*, **82**, 318 (1927).

[37] Bogart, R., Sperling, G., Barnes, L. L., and Asdell, S. A., *Am. J. Physiol.*, **128**, 355 (1940).

[38] Slonaker, J. R., *Id.*, **89**, 406 (1929).

Reproduction (the gestation not lactation part of reproduction) not only stimulates the growth of the maternal organism but it also stimulates further reproduction. Reproduction stimulates further reproduction because[39] "breeding promotes a greater harmony between the ovaries and other glands of internal secretion". The conclusions of the Asdell group are illustrated graphically in Fig. 14.21a and b.

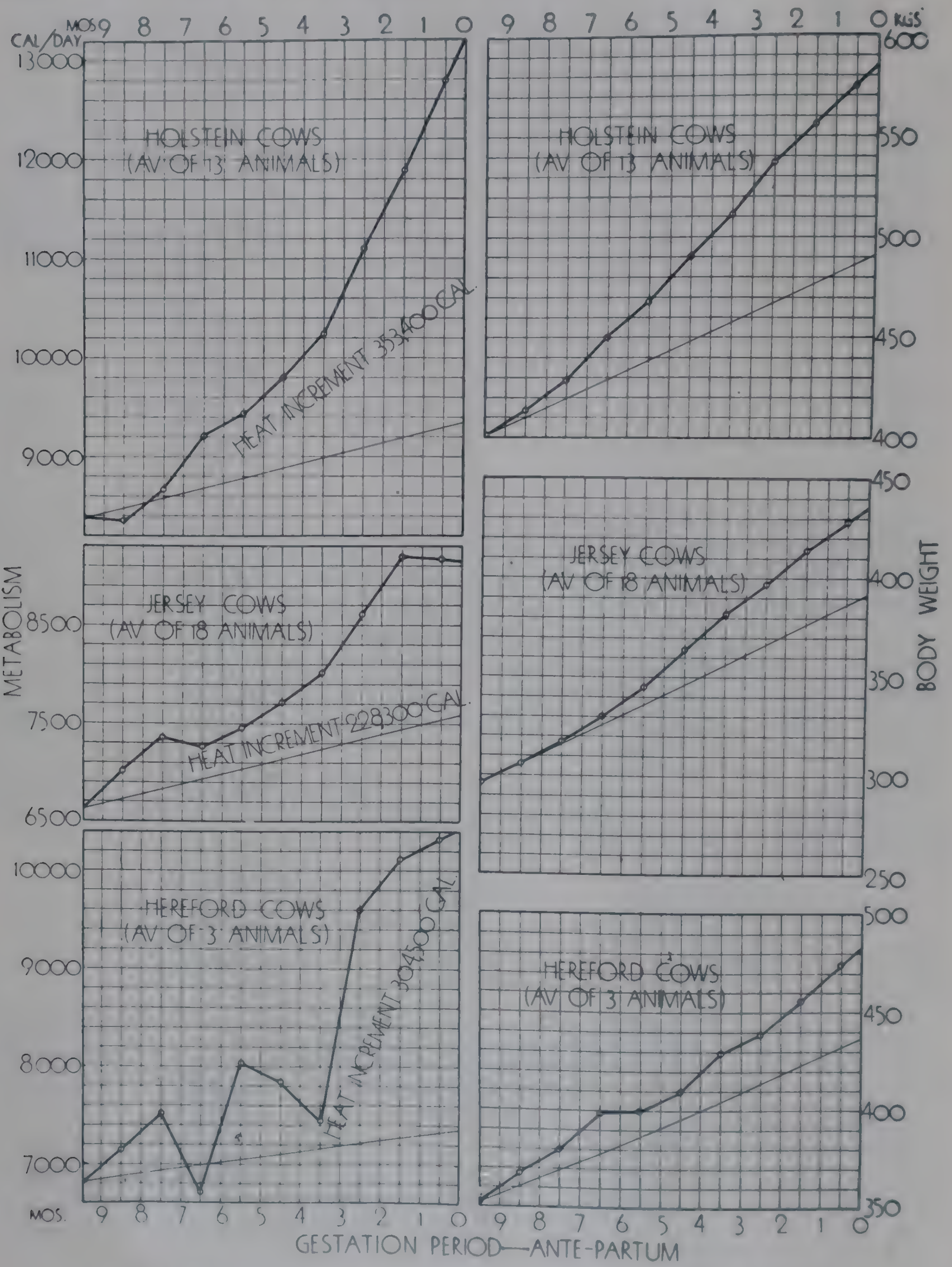

Fig. 14.23a. Heat and weight increments of gestation of cattle.

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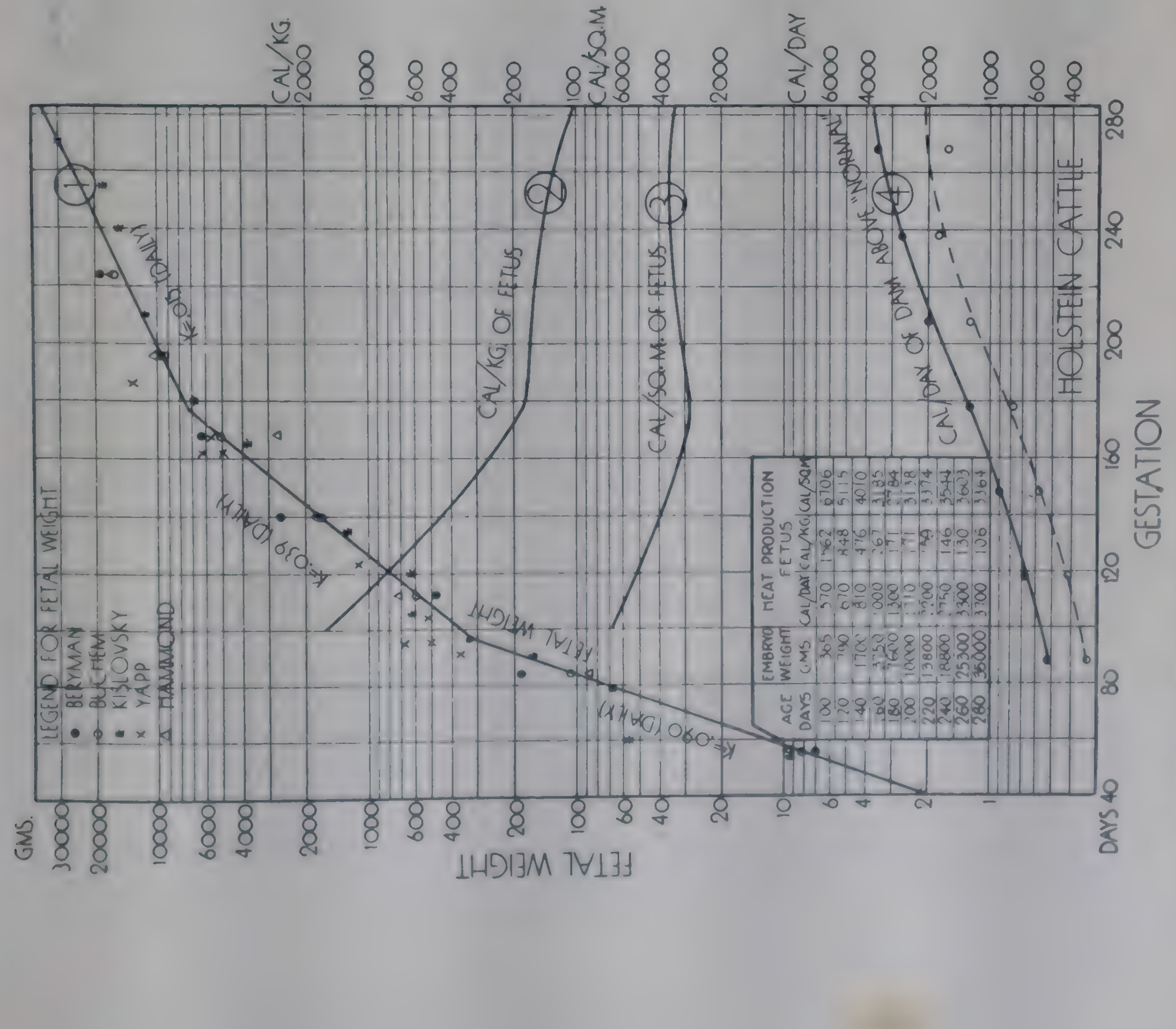
[39] Asdell, S. A., Bogart, R., and Sperling, G., "Influence of age and rate of breeding upon ability to reproduce," Cornell Univ. Memoir, p. 238, 1941.



AGE DAYS	EMBRYO WEIGHT GMS	HEAT PRODUCTION FETUS CAL/DAY	CAL/KG	CAL/SQM
100	365	570	1562	6706
120	790	670	848	5115
140	1700	810	476	4010
160	3750	1000	267	3185
180	7600	1300	171	2784
200	10000	1710	171	3138
220	13800	2000	145	3374
240	18800	2750	146	3544
260	25300	3300	130	3603
280	35000	3700	106	3364

Fig. 14.23b. Heat and weight increments of gestation of cattle.

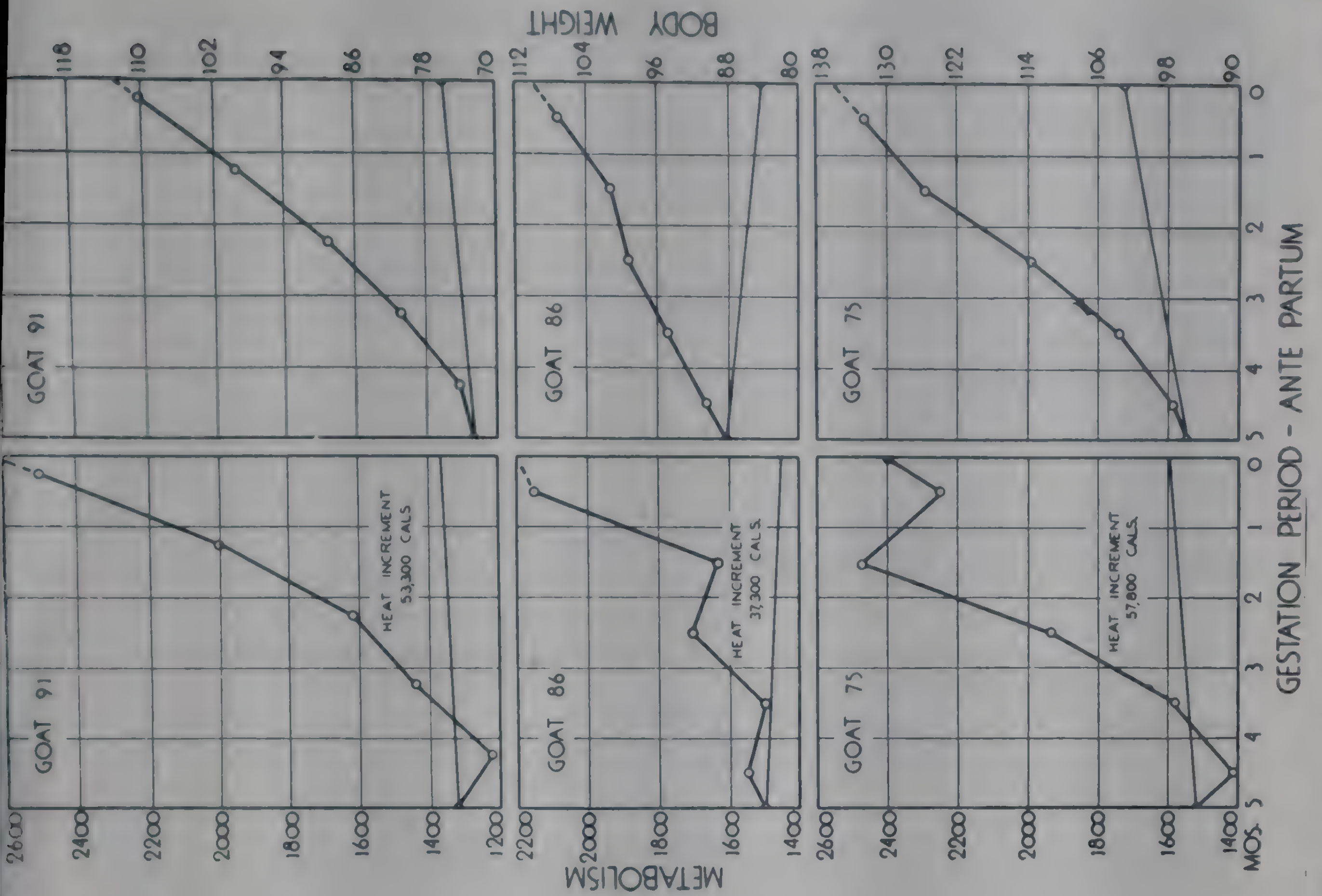


Fig. 14.23c. Heat and weight increments of gestation of goats.

14.8: Estimating the heat increment of gestation and total prenatal heat production. Fig. 14.17, representing the relation between birth weight and the heat increment of gestation, is necessarily crude because of the indirect method of estimating the heat increment of gestation and because of its mixed significance.

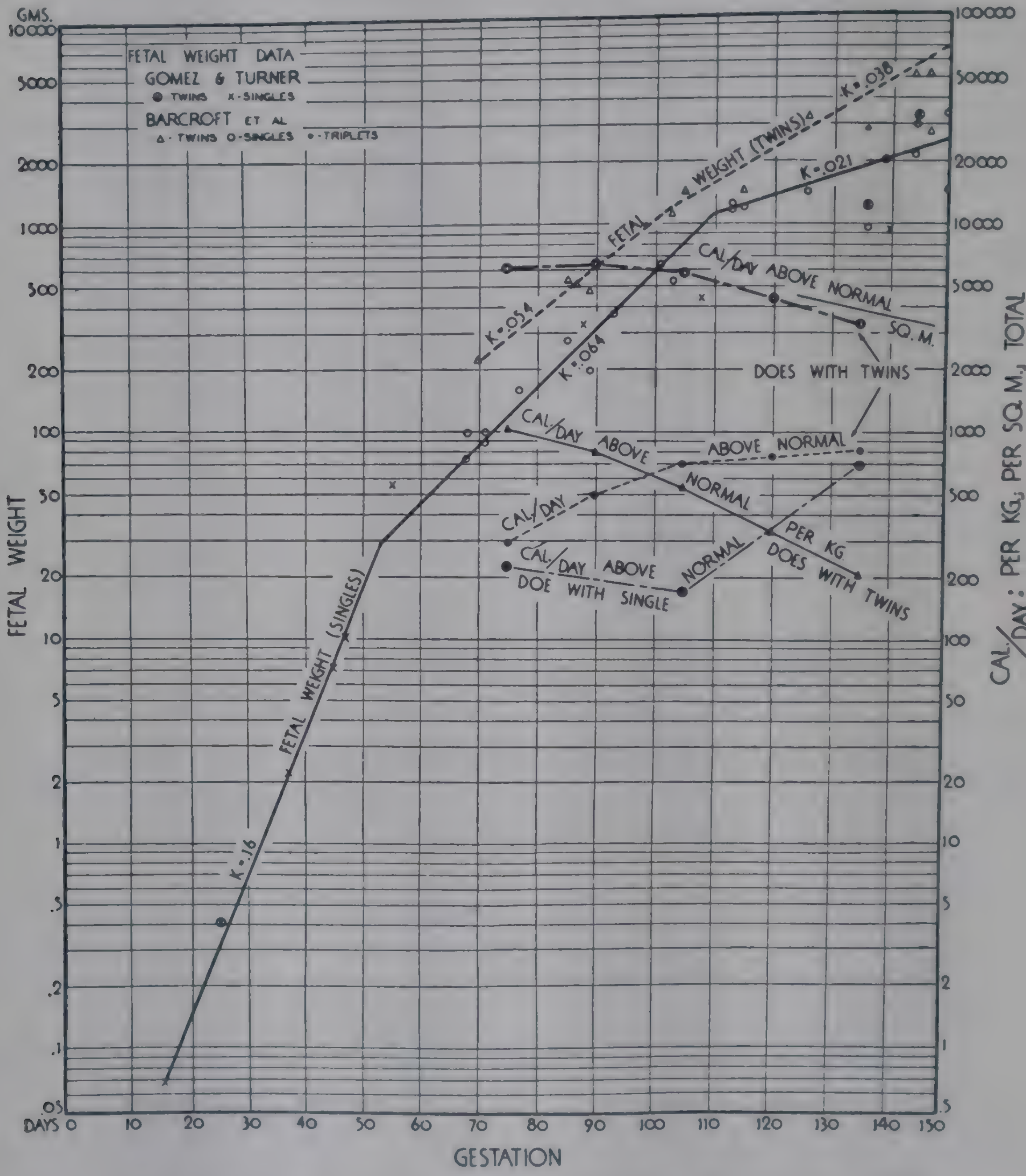


Fig. 14.23d. Heat and weight increments of gestation of does.

The simplest situation is that of the heat increment of incubation of the bird embryo. Here the total heat production, that is, the heat increment of incubation, is virtually the heat production of the bird embryo. This heat increment is shown (Fig. 14.22a) to be approximately 20 Cal for the chick embryo of the domestic fowl: about 20 Cal heat is dissipated during the production of a 40-Cal chick-embryo tissue. These 20 Cal represent the energy cost of maintenance of the formed embryo (Ch. 3) and perhaps of the "work" of growth. This is simple.

The situation is much more complex for intrauterine growth of mammals. The embryo, or fetus, is a small part of the mother whose metabolism is measured. As previously explained, the maternal organism undergoes profound metabolic changes involving the metabolism-stimulating endocrines during gestation, so that the heat increment of gestation is by no means the heat production of the embryo and fetus. The situation is further complicated if the mother is young and is growing herself. Yet Figs. 14.22b and c and 14.23 are based on just such data on the heat increments of gestation of young primapara.

The method of obtaining the heat increment of gestation is illustrated in these figures. The time curves for metabolism and for weights of the nongestating animals are extrapolated by straight lines to the weight and metabolism of the animals shortly after parturition, and the areas between the extrapolated lines and the observed lines for metabolism represent the heat increments of gestation. It is these heat increments of gestation that are given in Table 14.6.

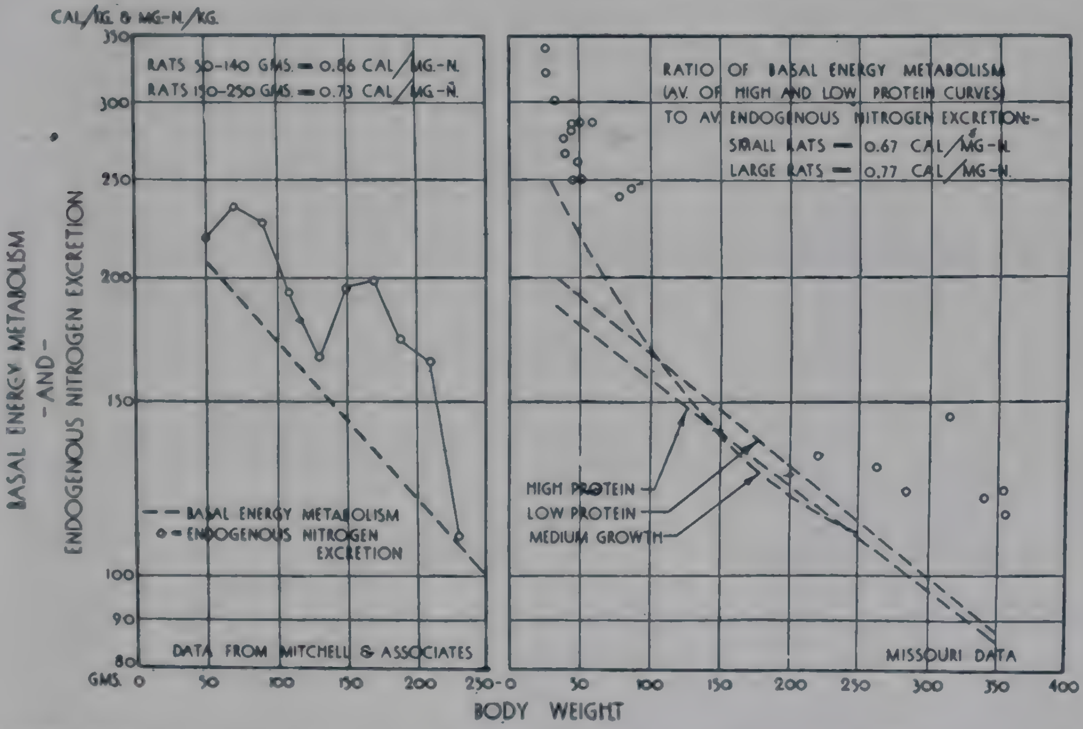


Fig. 14.24a. Demonstrates on semi-log paper the parallelism of the apparent endogenous nitrogen excretion and basal metabolism in rats of different body weight.

In spite of the crudeness of estimating the heat increment of gestation and their confused significance, the distribution of the data in Fig. 14.17 is quite orderly, and is apparently satisfactory for a first estimate relating prenatal heat production to birth weight.

In this connection the prenatal age curves of growth in weight (Figs. 14.23b and 14.23d) have some inherent interest. The values of k, the slopes of the curves, represent the instantaneous relative growth rate per day. Thus when the value of k is 0.16, the instantaneous growth rate is 16 per cent per day (Ch. 16).

When the heat increment of gestation is represented in terms of Cal/kg/day or Cal/sqm/day the resulting ratios are, as might be expected, unreasonably high (cf. Barcroft's direct measurements plotted in Fig. 14.18), since we measured not the heat production of the embryo or fetus but the heat increment of gestation, of which the heat production of the young is only one component.

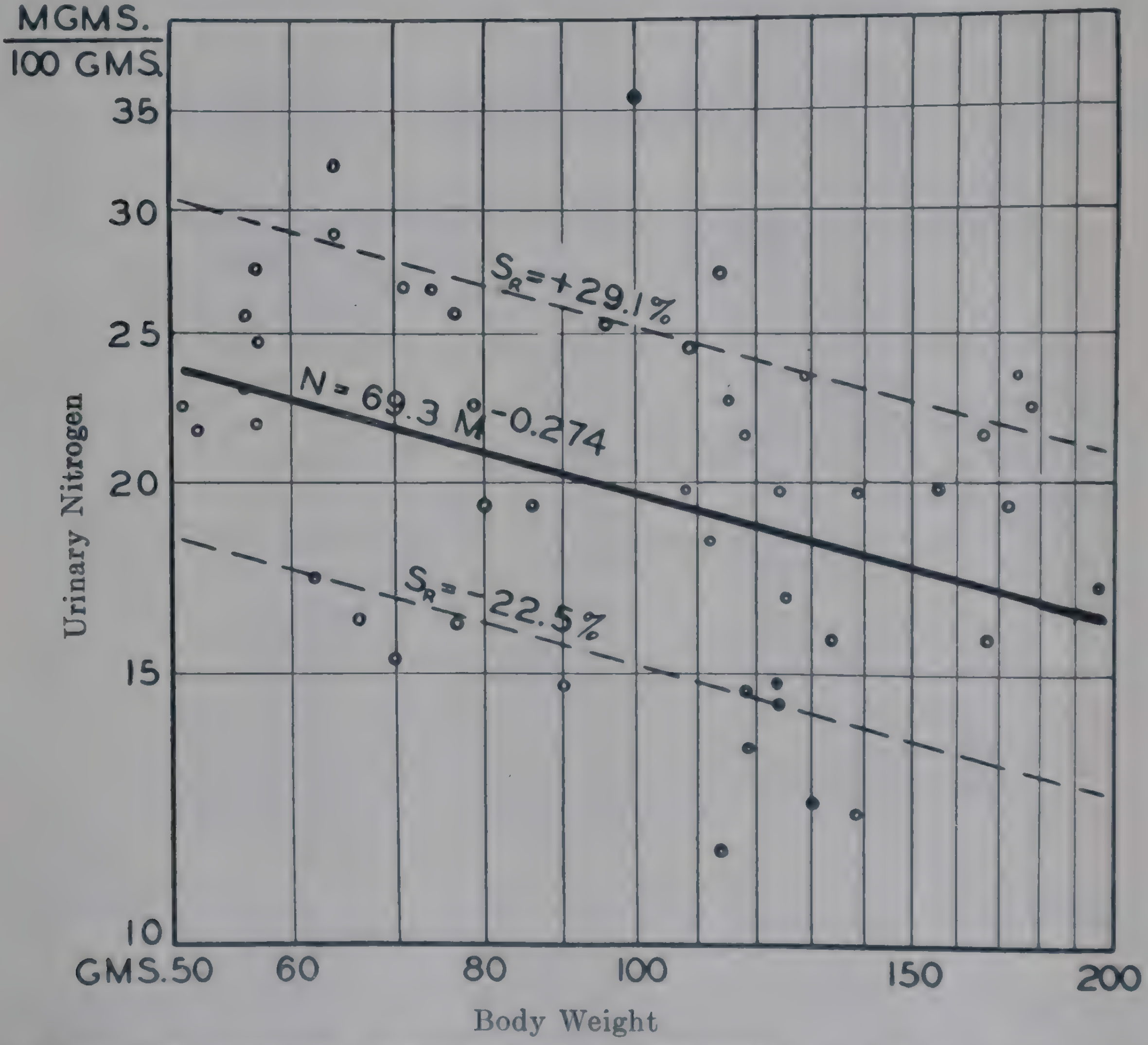


Fig. 14.24b. The apparent endogenous nitrogen excretion in rats varies with the 1.00 − .274 = 0.726 power of body weight.

14.9: Endogenous nitrogen excretion during growth. As previously explained (Ch. 13), the ratio of endogenous nitrogen to basal metabolism in *mature animals of different species* is approximately constant, 2 mg N/Cal; and the endogenous nitrogen, like basal metabolism, increases with approximately the 0.7 power of body weight. What is the relation between endogenous nitrogen and basal metabolism during growth? The writer believes that, following the age of natural weaning, they both tend to vary with 0.5 to 0.6 power of the body weight and that the ratio N/Cal is approximately constant. However, one cannot be certain for several reasons, one being that the basal metabolism and endogenous nitrogen concepts do not have the same significance in rapidly growing as in mature animals. One can only speak of *apparent* endogenous and basal metabolism. It is evidently difficult to attain an endogenous nitrogen level without disturbing normal growth. Moreover, the apparent endogenous level is influenced by many factors[40]: dietary protein level and quality before and during the period of specific nitrogen starvation, age, and so on, as indicated by Figs. 13.19, 14.24, and 14.25.

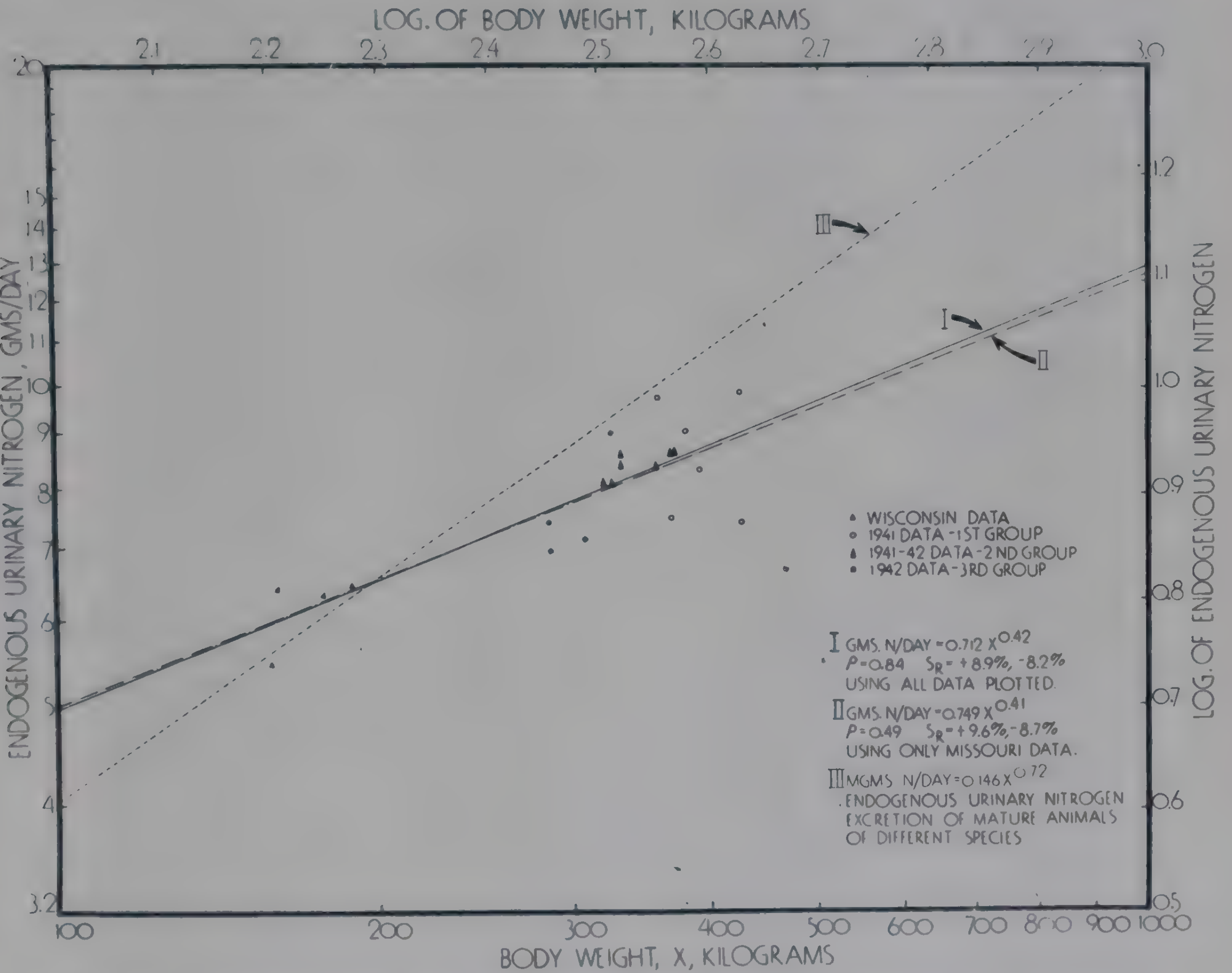


Fig. 14.24c. The apparent endogenous nitrogen excretion seems in this case to vary with the 0.42 power of body weight in growing Holstein cattle. Chart by Eric Swanson and H. A. Herman.[42]

Other conditions being equal, the lowest (endogenous) nitrogen excretion is attained not on a "protein-free" diet (0.5 mg N/gram air-dried food), but on one containing 5 to 6 mg N in the form of egg yolk per gram air-dried food (Mitchell).

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[40] Ashworth, U. S., and Brody, S., Mo. Agr. Exp. Sta. Res. Bulls., 189, 190, 1933. Ashworth, *Id.*, 223, 228, 1935. Mitchell, H. H., and Hamilton, "The biochemistry of amino acids," New York, 1929. Smuts, D. B., *J. Nut.*, **9**, 403 (1935).

The nitrogen excretion on a N-poor diet often continues to decline for 60 days[40,41]. Employing such techniques, the ratio of the *apparent* endogenous nitrogen to the *apparent* basal metabolism in young rats may be reduced to 1.5 or even to 1.0 mg N per Cal heat production. Such dietaries, of course, disturb the growth process.

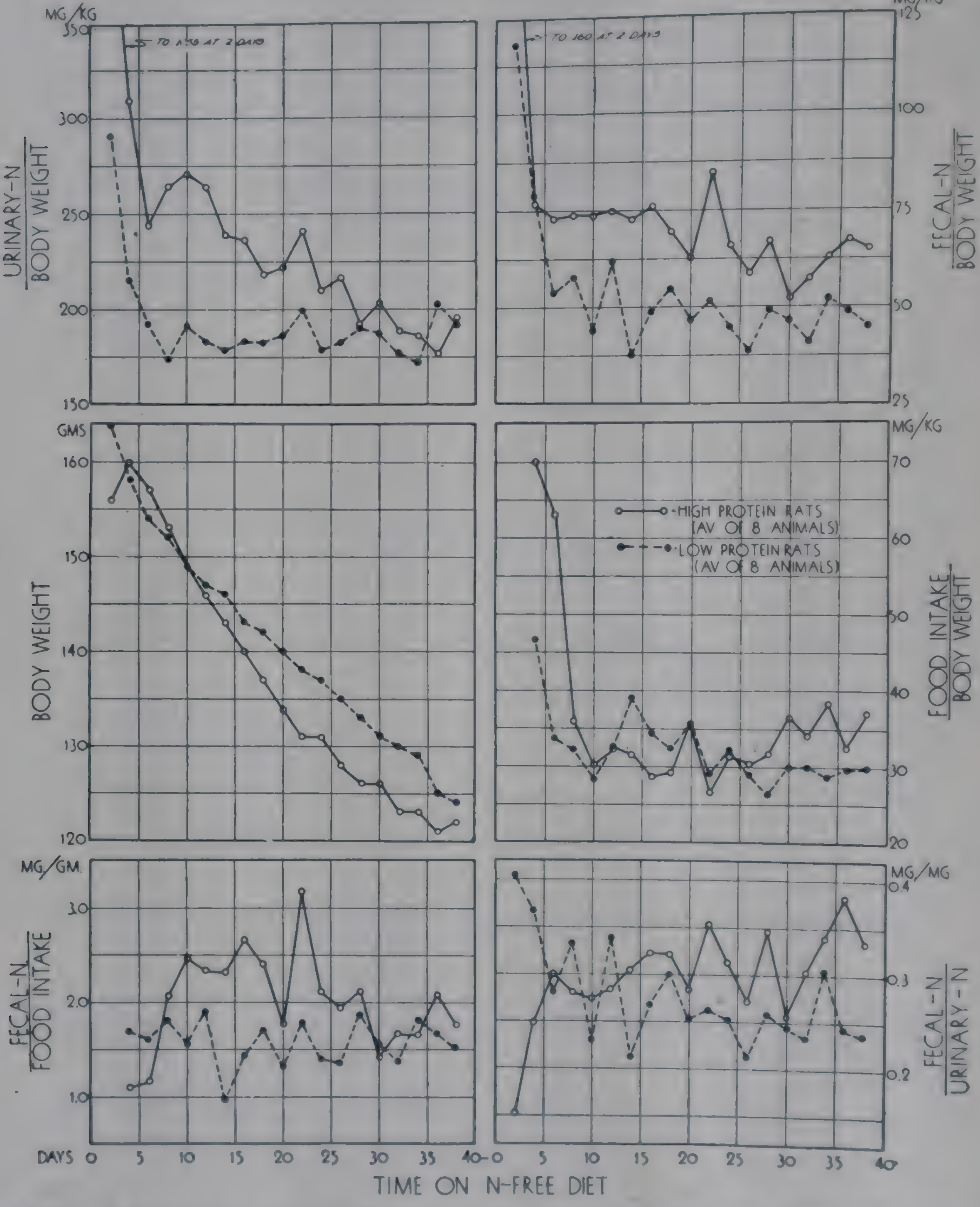

Fig. 14.25a. Influence of protein level (prior to the specific nitrogen inanition diet) on the course of nitrogen excretion.

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[41] Deuel, H. J., Sandiford, I. and K., and Boothby, W. M., *J. Biol. Chem.*, **76**, 391 (1928); Smith, M., *Id.*, **68**, 15 (1925). Ashworth and Brody, [40].

The above discussion makes it evident that it is a technically difficult problem to obtain data on endogenous nitrogen in normally growing animals. Nevertheless, the closeness of correlation between basal energy and endogenous nitrogen seems unmistakeable. The following illustrate the above discussion.

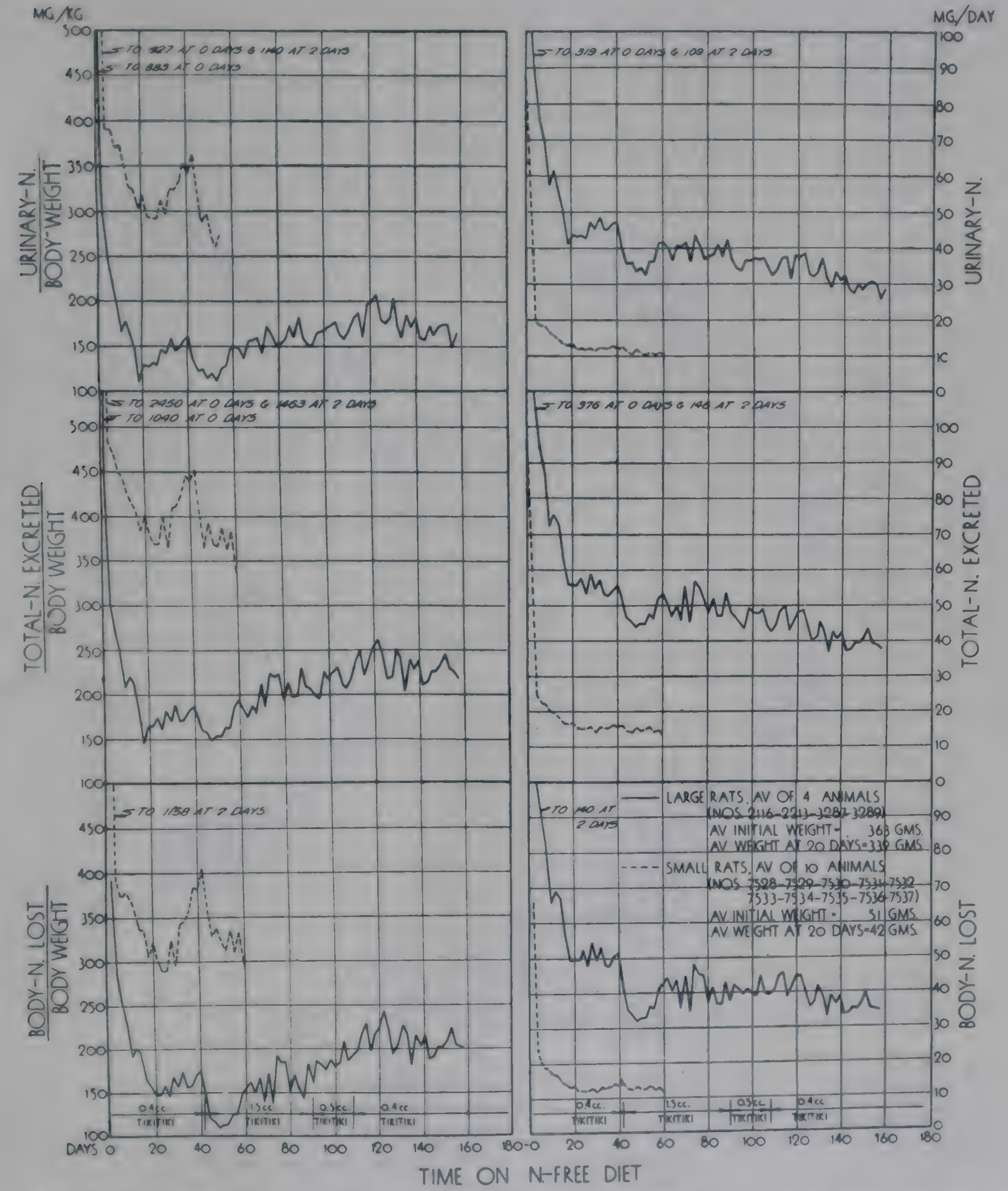

Fig. 14.25b. Influence of body weight (age) on the course of nitrogen excretion—on the time required to attain the apparent endogenous level.

Fig. 14.24a shows the parallelism of "basal" energy metabolism and endogenous nitrogen excretion (plotted on arithlog grid) of rats. Fig. 14.24b shows that the endogenous N excretion per unit weight declines with $M^{-0.274}$

or increases with $M^{0.726}$ (M is used in the chart to represent body weight instead of the usual W). This value of the slope is unexpectedly high for *growing* animals; it is close to that for mature animals of different species (Fig. 13.14).

Fig. 14.24c, shows[42] (on a log-log grid) that the endogenous nitrogen in growing Holstein heifers increases with only the 0.42 power of body weight, an unexpectedly low value.

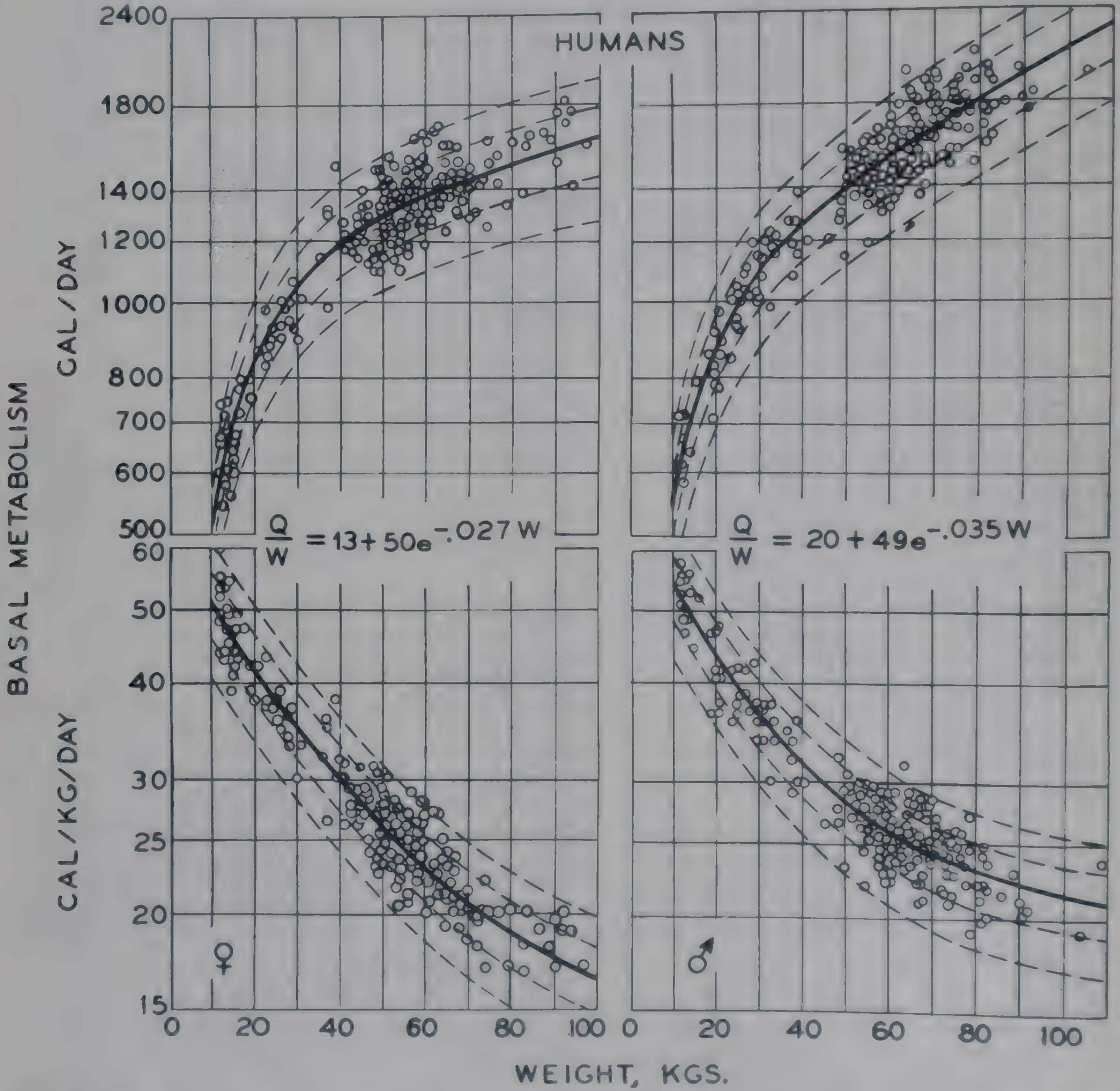

Fig. 14.26. Basal metabolism per unit weight, Q/W, of humans as function of body weight during growth. The heavy curve represents the given equation, the broken curves represent 10 and 20 per cent deviations from the average. 75 per cent of the data fall within ±10 per cent of the average curve, and 99.5 per cent of the data fall within ±20 per cent of the average curve. The data points are based on reports by Benedict, F. G., *Am. J. Physiol.*, **85**, 607 (1928), Benedict and Talbot, F. B., Carnegie Inst. Washington, Pub. 302 (1921), Harris, J. A., and Benedict, Id., Pub. 279, 1919, Boothby, W. M., and Sandiford, I., *J. Biol. Chem.*, **54**, 791 (1922).

The difference in slope for the growing cattle and rats is probably due to differences in experimental treatment, because as previously noted, the

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[42] Swanson, Eric, and Herman, H. A., Mo. Agr. Exp. Sta. Res. Bull. 382, 1943.

apparently endogenous nitrogen is sensitive to many factors, any one of which may affect the result. This is especially true of cattle with the rapid age changes in the digestive system and character of diet consumed. The writer feels that 0.4 is too low for the slope and that it will ultimately be shown to be nearer 0.6 (as for resting metabolism).

Figs. 14.25a and b show how the excretion of total N, N per unit body weight, and body weight vary with time on the low N diet, and the influence of protein level before the fast, and of body weight, on the shape and level of the N-excretion curves. The problem of the relation of endogenous nitrogen to body weight during growth is by no means solved, but we have here a beginning indicating that endogenous N and basal metabolism during growth both follow the same course, *i.e.*, that as a general rule both tend to increase with approximately the 0.6 power of body weight as contrasted to the 0.7 power of body weight for mature animals of different species.

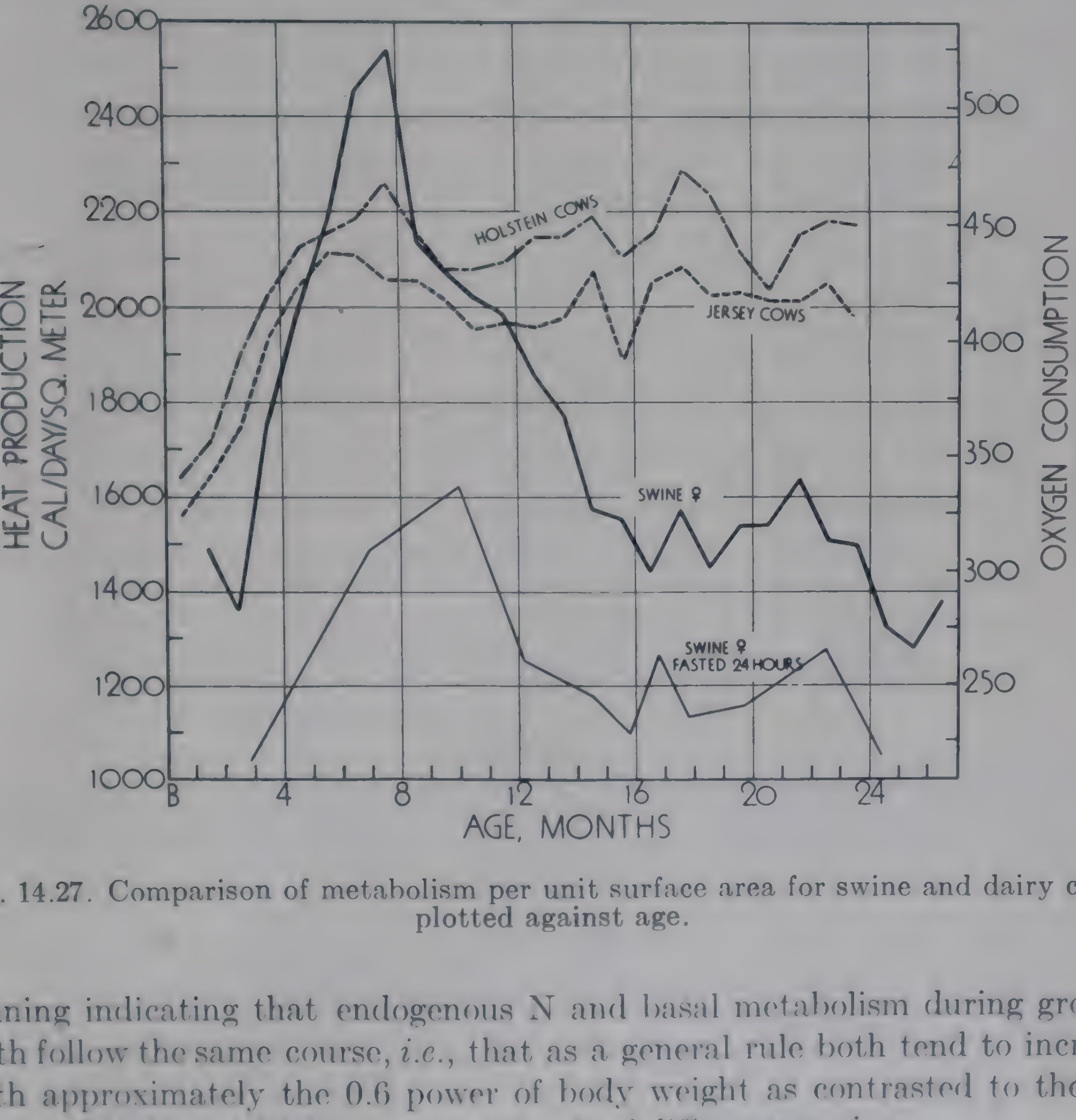

Fig. 14.27. Comparison of metabolism per unit surface area for swine and dairy cattle plotted against age.

14.10: Metabolism per unit weight as function of weight and of age during rapid growth. The preceding analysis of metabolism was concerned with surface area or with W^b as reference base. We found that the numerical value of b, when using W^b as base, is approximately 0.7 for mature animals of different species and approximately 0.6 for the same animals when growing.

In addition we employed[43] simple weight, $W^{1.0}$, or m, as reference base in the form of the relation

$$Q/m = ae^{-kt} + c$$

or

$$Q/m = ae^{-km} + c$$

in which Q is heat production for body weight m and age t; k is the relative (or percentage when multiplied by 100) decline in Q/m with increasing age, t, or weight, m; a and c are constants, c being the asymptote which Q/m approaches as a limit. The constant c may be dropped for a short segment of the $Q/m - m$ or $Q/m - t$ curve. These equations, of course, say that the heat production per unit body weight declines exponentially (Chs. 5, 16) with increasing age or weight.

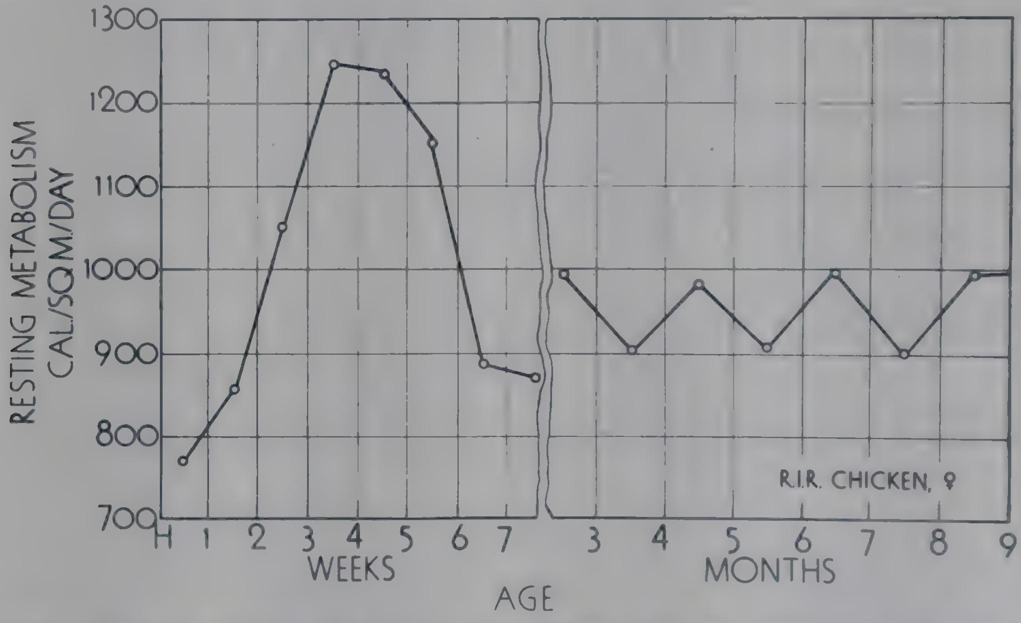

Fig. 14.28. Resting metabolism per unit surface area as function of age in Rhode Island Red chickens. (Surface area was computed from the equation, surface area in sq. cm. = 8.19 x (body weight in gms)$^{0.705}$.) The resting metabolism was computed on the assumption that 1 liter of oxygen had a heat equivalent of 4.9 Cal.

An application of the above equations to Q/m values during growth is presented in Fig. 14.26, and prediction values based on such analysis are given in Table 14.7 and those following it. Figs. 18.7 and 18.8 (Ch. 18), illustrate the life curves of the Q/m ratios. The Q/m ratio is there seen to rise postnatally until full homeothermy is attained, and declines thereafter to c as limiting value, except for a brief and relatively slight flare-up during puberty.

14.11: Summary and conclusions. While the ratio of metabolism per unit surface area, or much more precisely per W^b, is approximately constant for mature animals of different homeotherms (Ch. 13), this is not the case for the same animals when growing. During growth the metabolism per unit area, or per W^b, shows a peak; and when the total metabolism is plotted against weight on a log-log grid, the curve shows a "break". Prior to this peak or break, the metabolism tends to be directly proportional to simple weight, $W^{1.0}$; thereafter to $W^{0.6}$ or, roughly, to surface area.

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[43] Mo. Agr. Exp. Sta. Res. Bulls. 166 and 176, 1937.

This metabolic peak or break raises questions concerning its meaning. Is it associated with puberty? weaning? change in growth rate? stabilization of the neuroendocrine-homeothermic system? An inspection of the position of the metabolic peak in different species shows many variations in relation to weaning and puberty. For instance, the peak coincides with both puberty and weaning in cattle (puberty and weaning coincide in cattle); it occurs in swine[44] at puberty (at 7 months, Fig. 14.27) but not at weaning (which occurs at approximately 2 months of age); it occurs in rats sometime between weaning and puberty (Fig. 14.1); it coincides in humans with weaning (2 to 3 years, prior to which age milk is an indispensable part of the diet) although a relatively insignificant pubertal peak (near age 13 years) has also been reported[45]; in chickens (Fig. 14.28) the metabolic peak occurs at the age of about one month[46, 47] while puberty occurs at, perhaps, 5 or 6 months. This species variation in the occurrence of the metabolic peak with respect to weaning and puberty indicates that weaning and puberty are not the "causes" of the peak. Moreover, on plotting metabolism per unit area and weight gain per unit area against age a parallelism is observed between the two[47], indicating that the rise and decline in metabolism per unit area tends to be associated with the rise and decline in growth rate per unit area.

It is, therefore, concluded that the position of the metabolic peak is not due to one "cause" but is the resultant of many factors—to puberty, to weaning, to changes in growth rate, but particularly to stabilization of the neuroendocrine-homeothermic system.

An interesting feature of early postnatal metabolism of rats is that the brain metabolism per unit *weight* appears to parallel the total body metabolism per unit *surface area* (see Sect. 17.4, relating brain weight to metabolic rate in different species).

The endogenous nitrogen expense during growth appears to parallel that of basal energy metabolism.

A very brief discussion, but with many tables, is presented (Sect. 14.10) on the relation of metabolism to age and to weight generalized by the equation $Q/m = a + be^{-kt}$ and $Q/m = a + be^{-km}$ in which Q/m represents heat production per unit weight, and t represents age. The applicability of this equation form to metabolism data is significant because it also represents growth relationships of other categories (Chs. 5, 16, 18, 19), particularly growth of neuroendocrine organs in relation to total body weight and age[43].

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[44] Brody, S., and Kibler, H. H., "Resting energy metabolism and pulmonary ventilation in growing swine", Id., Res. Bull. 380, 1944.

[45] See especially, MacLeod, Grace, "Studies of the normal basal energy requirements", Dissertation, Columbia University, 1924, and Du Bois, E. F., "Basal Metabolism in Health and Disease", Lea and Febiger (several editions).

[46] Mitchell, H. H., Card, L. E., and Haines, W. T., *J. Agr. Res.*, **34**, 945 (1927).

[47] Kibler, H. H., and Brody, S., *J. Nut.*, **28**, 27 (1944).

Fig. 13.9 (Ch. 13) might be included in this chapter; it shows the metabolism curves of the *same growing* animals alongside the curve relating metabolism to weight of *mature* animals of different species; so could Figs. 18.7 and 18.8 (Ch. 18) which present metabolic life curves.

Discussion and data are presented on prenatal heat production and on the heat increment of gestation, and on their relation to the weight of the newborn. The prediction values discussed are given in the following appendix.

Table 14.1. Growth and metabolism of Rhode Island Red chickens.[1]
(24-hour fasting data given on starred lines.)

Age Period		Females (Average per Chicken)			Males (Average per Chicken)		
		Body weight (gm)	Cal.[2] per day	Cal./sq.m.[3] per day	Body weight (gm)	Cal.[2] per day	Cal./sq.m.[3] per day
Week	H-1	43	8.8	774	48	9.1	740
	1-2	54	11.6	862	74	16.1	965
	2-3	91	20.4	1056	124	26.0	1086
	3-4	152	34.5	1250	201	40.2	1197
	4-5	216	43.8	1240	294	58.2	1328
	5-6	299	51.2	1155	410	65.9	1191
	6-7	351	44.3	893	471	61.5	1009
	7-8	392	47.0	877	509	60.3	937
Month	2-3	679	78.8	1001	821	85	920
	*2-3	631	59.4	794	728	63	866
	3-4	1152	104	913	1436	138	1037
	*3-4	1048	83	778	1300	100	806
	4-5	1602	142	992	2023	190	1125
	*4-5	1479	113	834	1914	161	990
	5-6	1724	139	917	2580	229	1143
	*5-6	1319	109	872	2470	185	952
	6-7	1784	156	1008	—	—	—
	*6-7	1679	134	906	—	—	—
	7-8	1925	149	913	—	—	—
	*7-8	1822	106	674	—	—	—
	8-9	2126	176	1003	—	—	—
	*8-9	1864	112	705	—	—	—
	9-10	2054	172	1008	—	—	—
	*9-10	1944	131	798	—	—	—
	10-11	1878	121	755	—	—	—
	*10-11	1818	99	633	—	—	—
	11-12	1931	161	983	—	—	—
	*11-12	1835	142	865	—	—	—
	12-13	2260	164	897	—	—	—
	*12-13	2084	113	773	—	—	—

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[1] For methods and equations see Kibler and Brody[47].

[2] The heat production was calculated on the assumption that 1 liter of oxygen has a heat equivalent of 4. Cal. for the fed chickens and 4.7 Cal. for the fasted chickens.

[3] Surface area was computed from the equation, surface area in sq. cm. = 8.19 (body weight in grams)$^{0.70}$ as determined for White Leghorn chickens by Mitchell ('30).

Table 14.1a. Growth and metabolism of albino rats
(Basal values are shown on starred lines.)

Litters				Females				Males			
Age (days)	Average per rat			Age (days)	Average per rat			Age (days)	Average per rat		
	Body weight (gm)	Cal.[1] / Day	Cal./sq.m.[2] / Day		Body weight (gm)	Cal.[1] / Day	Cal./sq.m.[2] / Day		Body weight (gm)	Cal.[1] / Day	Cal./sq.m.[2] / Day
1	5.64	1.51	456	24	34.0	7.9	779	24	35.5	8.0	771
2	6.21	2.09	596	26	39.6	10.3	921	26	39.1	11.4	1038
3	7.07	2.31	614	28	46.0	12.4	1010	28	44.7	12.6	1053
4	8.37	2.33	552	30	52.2	14.8	1117	30	51.7	15.1	1114
5	9.74	2.70	581	32	60.8	16.5	1130	32	60.4	16.4	1130
6	10.7	3.11	635	*32	50.5	13.6	1045	*32	56.7	12.3	878
7	12.2	3.48	666	34	68.8	19.4	1203	34	68.4	17.6	1084
8	13.3	2.98	531	*34	57.2	12.4	880	*34	58.7	15.0	1048
9	14.2	2.55	437	36	76.6	19.8	1193	36	78.1	19.1	1126
10	15.5	3.22	520	*36	75.9	16.8	998	*36	74.2	16.5	995
11	16.3	2.97	466	40	93.3	23.2	1210	40	101.0	24.2	1204
12	17.4	3.41	512	*40	85.6	18.6	1022	*40	89.5	20.1	1080
13	18.9	4.06	578	45	112	26.7	1241	45	128	28.0	1198
14	19.8	4.05	559	*46	104	22.9	1119	*46	118	24.3	1094
15	20.8	4.24	564	50	119	26.2	1171	50	147	29.3	1149
16	21.7	4.74	616	*51	118	22.5	1015	*51	137	23.4	962
17	22.9	4.52	569	55	138	25.1	1035	55	167	28.4	1029
18	23.6	4.73	586	*56	127	23.2	998	*56	161	26.8	991
19	24.4	4.83	584	60	153	27.4	1048	60	201	30.8	991
20	25.4	5.29	624	65	162	27.6	1021	65	221	33.1	1002
21	28.9	6.53	713	*66	149	23.4	912	*66	209	27.6	867
22	32.1	7.02	714	74	171	27.7	987	74	249	33.6	946
				*76	162	22.4	824	*76	242	30.2	865
				85	180	25.6	884	85	269	32.9	882
				*87	178	23.0	800	*87	264	31.6	857
				100	192	27.7	917	100	293	33.9	862
				*101	174	23.6	829	*101	276	31.9	843
				120	197	27.1	880	120	310	33.7	826
				*121	185	23.8	806	*121	296	31.4	797

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[1] The heat production was calculated on the assumption that 1 liter of oxygen had a heat equivalent of 4.7 Cal for the litters and 4.9 Cal for the older rats. A value of 4.7 Cal was also assumed for the fasted rats.

[2] Surface area was computed from the equation, surface area in square meters = $0.0011\ (\text{weight in gm.})^{0.63}$.

Table 14.2. Prediction Table for Resting Energy Maintenance Cost and Ventilation Rate in Growing Holstein Cattle.

Body Weight		Approximate age (mos)	Energy Maintenance Cost per 24 hours							Oxygen Consumption Per 24 hours (S.T.P.)				Ventilation Rate Per Minute (S.T.P.)				Ventilation rate (liters per sq. m. per day)	Ratio of oxygen Consumption to Ventilation Rate
			Calories			B.T.U.		Equivalent[2] in *TDN*	Total *TDN*[3] consumed, (lbs)	Liters		Cu. ft.		Liters		Cu. ft.			% $\frac{O_2\text{, consumed}}{\text{Air, inhaled}}$
(kg)	(lbs)		Total	Per Kg.	Per Sq. M.[1]	Total	Per lb.			Total	Per Kg.	Total	Per Lb.	Total	Per Kg.	Total	Per Lb.		
40	88.2	.4	1875	46.9	1600	7440	84	1.0	—	389	9.7	13.7	.155	14.3	.357	.51	.0058	17390	1.89
50	110.2	1.1	2254	45.1	1700	8940	81	1.2	1.4	467	9.3	16.5	.150	17.0	.340	.60	.0054	18260	1.91
75	165.3	2.7	3137	41.8	1870	12450	75	1.7	2.5	650	8.7	22.9	.139	23.3	.312	.82	.0050	19940	1.94
100	220.5	3.8	3965	39.7	2060	15730	71	2.2	3.8	822	8.2	29.0	.131	29.1	.291	1.03	.0047	21200	1.96
125	275.0	4.8	4757	38.1	2090	18880	68	2.6	4.9	986	7.9	34.8	.126	34.6	.276	1.22	.0044	22230	1.98
150	330.7	6.0	5153	34.4	2100	20450	62	2.8	5.8	1068	7.1	37.7	.114	39.9	.266	1.41	.0043	23160	1.86
175	385.8	7.2	5649	32.3	2120	22420	58	3.1	6.2	1171	6.7	41.4	.107	44.9	.256	1.59	.0041	23900	1.81
200	440.9	8.2	6119	30.6	2130	24280	55	3.4	6.6	1268	6.3	44.8	.102	49.8	.249	1.76	.0040	24600	1.77
250	551.1	11.5	6990	28.0	2120	27740	50	3.9	7.4	1449	5.8	51.2	.093	59.2	.236	2.09	.0038	25810	1.70
300	661.4	14.2	7795	26.0	2170	30930	47	4.3	8.4	1616	5.4	57.1	.086	68.2	.227	2.41	.0036	26850	1.65
350	771.6	16.8	8547	24.4	2140	33910	44	4.7	10.1	1771	5.1	62.5	.081	76.9	.220	2.72	.0035	27770	1.60
400	881.8	19.6	9255	23.1	2160	36720	42	5.1	11.4	1918	4.8	67.7	.077	85.2	.213	3.01	.0034	28540	1.56
450	992.1	22.0	9929	22.1	2160	39400	40	5.5	11.8	2058	4.6	72.7	.073	93.4	.208	3.30	.0033	29300	1.53
500	1102.0	24.0	10570	21.1	2180	41940	38	5.8	12.9	2191	4.4	77.4	.070	101.3	.203	3.58	.0032	29960	1.50
550	1213.0	—	11190	20.3	—	44400	37	6.2	—	2320	4.2	81.9	.068	109.1	.198	3.85	.0032	30580	1.48
600	1323.0	—	11790	19.7	—	46780	35	6.5	—	2444	4.1	86.3	.065	116.7	.195	4.12	.0031	31170	1.45

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[1] Surface area was computed from the equation, surface area in sq. meters = 0.15 (weight in kg.)$^{0.56}$. See Mo. Res. Bul. 89, p. 10. The heat production was computed on the assumption that one liter of oxygen has a heat equivalent of 4.825 Cal. This value is probably slightly high for the younger calves taking milk and low for the older heifers. The error incurred by this assumption is well within the experimental error.

[2] Computed on the assumption that 1 lb. *TDN* (total digestible nutrients) is equivalent to 1814 Cal or 1 gm. of *TDN* to 4 Cal.

[3] Interpolated from page 8 of Mo. Exp. Sta. Bul. 338 covering feed records for large groups (35 to 87 animals). This represents not resting energy metabolism computed from O_2 consumption but actual total TDN consumed.

Table 14.3. Prediction Table for Resting Energy Maintenance Cost and Ventilation Rate in Growing Jersey Cattle.

Body Weight		Energy Maintenance Cost per 24 hours							Oxygen Consumption Per 24 Hours (S.T.P.)				Ventilation Rate Per Minute (S.T.P.)				Ratio of oxygen consumption to ventilation rate
		Calories			B.T.U.		Equivalent[2] *TDN* (lb)	Total *TDN*[3] consumed (lbs)	Liters		Cu. ft.		Liters		Cu. ft.		% O₂, Liters consumed / Air, Liters inhaled
(kgs)	(lbs)	Total	Per Kg.	Per Sq. M.[1]	Total	Per Lb.			Total	Per Kg.	Total	Per Lb.	Total	Per Kg.	Total	Per Lb.	
25	55.1	1303	52.1	1420	5169	94	.7	—	270	10.8	9.5	.172	10.0	.402	.36	.0064	1.88
50	110.2	2364	47.3	1770	9381	85	1.3	1.9	490	9.8	17.3	.157	16.6	.331	.59	.0053	2.05
75	165.3	3329	44.4	1970	13210	80	1.8	3.0	690	9.2	24.4	.148	22.2	.296	.78	.0047	2.16
100	220.5	3908	39.1	2050	15510	70	2.2	4.1	810	8.0	28.6	.130	27.3	.273	.96	.0044	2.06
125	275.6	4439	35.5	2050	17610	64	2.4	4.8	920	7.4	32.5	.118	32.0	.256	1.13	.0041	2.00
150	330.7	4922	32.8	2010	19530	59	2.7	5.2	1020	6.8	36.0	.109	36.5	.243	1.29	.0039	1.94
175	385.8	5356	30.7	1970	21250	55	3.0	5.5	1110	6.3	39.2	.102	40.8	.233	1.44	.0037	1.89
200	440.9	5790	29.0	1990	22970	52	3.2	6.2	1200	6.0	42.4	.096	44.9	.225	1.59	.0036	1.86
250	551.1	6562	26.2	2020	26040	47	3.6	7.3	1360	5.4	48.0	.087	52.7	.211	1.86	.0034	1.79
300	661.4	7238	24.1	2010	28710	43	4.0	8.8	1500	5.0	53.0	.080	60.1	.200	2.12	.0032	1.73
350	771.6	7913	22.6	1960	31400	41	4.4	9.6	1640	4.7	57.9	.075	67.2	.192	2.37	.0031	1.69
400	881.8	8492	21.2	1940	33670	38	4.7	—	1760	4.4	62.2	.071	74.0	.185	2.61	.0030	1.65
450[4]	992.1	9071	20.2	—	35990	36	5.0	—	1880	4.2	66.4	.067	80.5	.179	2.84	.0029	1.62
500[4]	1102.0	9650	19.3	—	38290	35	5.3	—	2000	4.0	70.6	.064	86.9	.174	3.07	.0028	1.60

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[1] Surface area was computed from the equation, surface area in sq. meters = 0.15 (weight in kg.)$^{0.56}$. See Mo. Res. Bul. 89, p. 10. The heat production was computed on the assumption that one liter of oxygen has a heat equivalent of 4.825 Calories. This value is probably slightly high for the younger calves taking milk and low for the older heifers. The error incurred by this assumption is well within the experimental error.

[2] Computed on the assumption that 1 lb. TDN (total digestible nutrients) is equivalent to 1814 Cal. or 1 gm. of TDN to 4 Cal.

[3] Interpolated from page 10 of Mo. Exp. Sta. Bul. 338 covering feed records for large groups (36 to 63 animals).

[4] Computations for these body weights are extrapolations beyond the range of actual data.

Table 14.4. Prediction Table for Resting Energy Maintenance Cost and Ventilation Rate in Growing Percheron Horses (Females). (Computed from Equations in Figs.)

Body Weight		Approximate age (mos)	Energy Maintenance Cost per 24 hrs.						Oxygen Consumption (S.T.P.)				Ventilation Rate (S.T.P.)					Ratio of oxygen consumption to ventilation rate
									Per 24 hours				Per minute				Per day	
			Calories			B.T.U.		Equivalent[3] in *TDN* (lbs)	Liters		Cu. ft.		Liters		Cu. ft.		Liters	% $\frac{O^2 \text{ consumed}}{\text{Air inhaled}}$
(kg)	(lbs)		Total[1]	Per kg.	Per sq. m.[2]	Total	Per lb.		Total	Per kg.	Total	Per lb.	Total	Per kg.	Total	Per lb.	Per sq. m.	
75	165.3	.1	3850	51.3	2540	15280	92	2.1	800	10.6	28.2	.171	28.7	.383	1.01	.0061	27220	1.93
100	220.5	.7	4497	45.0	2470	17840	81	2.5	930	9.3	32.9	.149	33.7	.337	1.19	.0054	26660	1.92
125	275.6	1.3	5073	40.6	2420	20130	73	2.8	1050	8.4	37.1	.135	39.2	.314	1.38	.0050	26940	1.86
150	330.7	1.8	5598	37.3	2380	22210	67	3.1	1160	7.7	41.0	.124	44.4	.296	1.57	.0047	27210	1.81
175	385.8	2.4	6083	34.8	2350	24140	63	3.4	1260	7.2	44.5	.115	49.3	.282	1.74	.0045	27410	1.78
200	440.9	2.9	6538	32.7	2320	25940	59	3.6	1360	6.8	47.8	.108	54.0	.270	1.91	.0043	27610	1.74
225	496.0	3.4	6968	31.0	2300	27650	56	3.8	1440	6.4	51.0	.103	58.5	.260	2.07	.0042	27770	1.71
250	551.1	4.0	7375	29.5	2280	29260	53	4.1	1530	6.1	54.0	.098	62.9	.252	2.22	.0040	27960	1.69
275	606.3	4.8	7765	28.2	2260	30810	51	4.3	1610	5.8	56.8	.094	67.1	.244	2.37	.0039	28080	1.67
300	661.4	6.0	8138	27.1	2240	32290	49	4.5	1690	5.6	59.6	.090	71.2	.237	2.51	.0038	28200	1.65
350	771.6	8.5	8845	25.3	2210	35100	46	4.9	1830	5.2	64.7	.084	79.0	.226	2.79	.0036	28400	1.61
400	881.8	14.0	9507	23.8	2180	37720	43	5.2	1970	4.9	69.6	.079	86.5	.216	3.05	.0035	28580	1.58
450	992.1	18.1	10130	22.5	2150	40200	40	5.6	2100	4.7	74.1	.075	93.8	.208	3.31	.0033	28780	1.55
500	1102	23.0	12450	24.9	2480	49400	45	6.9	2580	5.2	91.1	.083	100.7	.201	3.56	.0032	28910	1.78
550	1212	26.0	13655	24.8	2560	54180	45	7.5	2830	5.1	100.0	.082	107.5	.195	3.80	.0031	29060	1.83
600	1323	29.0	14858	24.8	2640	58960	45	8.2	3080	5.1	108.7	.082	114.0	.190	4.03	.0030	29180	1.88
650	1433	33.0	16055	24.7	2710	63710	44	8.8	3330	5.1	117.5	.082	120.4	.185	4.25	.0030	29300	1.92
700	1543	40.0	17252	24.6	2780	68460	44	9.5	3580	5.1	126.3	.082	126.6	.181	4.47	.0029	29400	1.96
750	1654	49.0	18448	24.6	2850	73200	44	10.2	3820	5.1	135.0	.082	132.7	.177	4.69	.0028	29510	2.00
800	1764	60.0	19638	24.5	2910	77920	44	10.8	4070	5.1	143.7	.081	138.6	.173	4.89	.0028	29590	2.04

Table 14.4 (cont'd) (Geldings).

(Computed from Equations in Figs.)

Body Weight		Approximate age (mos)	Energy Maintenance Cost per 24 hrs.						Oxygen Consumption (S.T.P.)				Ventilation Rate (S.T.P.)					Ratio of oxygen consumption to ventilation rate
									Per 24 hours				Per minute				Per day	
			Calories			B.T.U.		Equivalent[3] in *TDN* (lbs)	Liters		Cu. ft.		Liters		Cu. ft.		Liters	
(kg)	(lbs)		Total[1]	Per kg.	Per sq. m.[2]	Total	Per lb.		Total	Per kg.	Total	Per lb.	Total	Per kg.	Total	Per lb.	Per sq. m.	% $\frac{O_2 \text{ consumed}}{\text{Air inhaled}}$
75	165.3	.1	3861	51.5	2540	15320	93	2.1	800	10.7	28.2	.171	28.7	.383	1.01	.0061	27220	1.94
100	220.5	.6	4484	44.8	2460	17790	81	2.5	930	9.3	32.8	.149	33.7	.337	1.19	.0054	26660	1.91
125	275.6	1.0	5036	40.3	2410	19980	72	2.8	1040	8.4	36.9	.134	39.2	.314	1.38	.0050	26940	1.85
150	330.7	1.6	5537	36.9	2360	21970	66	3.1	1150	7.6	40.5	.122	44.4	.296	1.57	.0047	27210	1.80
175	385.8	2.2	5981	34.2	2310	23730	62	3.3	1240	7.1	43.8	.114	49.3	.282	1.74	.0045	27410	1.75
200	440.9	2.8	6430	32.2	2280	25510	58	3.5	1330	6.7	47.1	.107	54.0	.270	1.91	.0043	27610	1.71
225	496.0	3.4	6837	30.4	2250	27130	55	3.8	1420	6.3	50.0	.101	58.5	.260	2.07	.0042	27770	1.68
250	551.1	4.0	7221	28.9	2230	28650	52	4.0	1500	6.0	52.8	.096	62.9	.252	2.22	.0040	27960	1.65
275	606.3	4.8	7588	27.6	2200	30110	50	4.2	1570	5.7	55.6	.092	67.1	.244	2.37	.0039	28080	1.63
300	661.4	6.0	7939	26.5	2180	31500	48	4.4	1640	5.5	58.1	.088	71.2	.237	2.51	.0038	28200	1.60
350	771.6	9.5	8602	24.6	2150	34130	44	4.7	1780	5.0	62.2	.081	79.0	.226	2.79	.0036	28400	1.56
400	881.8	14.0	9221	23.0	2120	36590	42	5.1	1910	4.8	67.5	.076	86.5	.216	3.05	.0035	28580	1.53
450	992.1	18.0	9803	21.8	2090	38900	40	5.4	2030	4.5	71.8	.072	93.8	.208	3.31	.0033	28780	1.50
500	1102	24.0	12029	24.1	2400	47730	43	6.6	2490	5.0	88.0	.080	100.7	.201	3.56	.0032	28910	1.72
550	1212	27.3	13461	24.5	2530	53410	44	7.4	2790	5.1	98.5	.081	107.5	.195	3.80	.0031	29060	1.80
600	1323	35.0	14917	24.9	2650	59190	45	8.2	3090	5.2	109.2	.083	114.0	.190	4.03	.0030	29180	1.88
650	1433	50.0	17892	25.2	2770	65040	45	9.0	3400	5.2	120.0	.084	120.4	.185	4.25	.0030	29300	1.96
700	1543	58.0	17890	25.6	2880	70990	46	9.9	3710	5.3	130.9	.085	126.6	.181	4.47	.0029	29400	2.03
750[4]	1654	—	19410	25.9	3000	77020	47	10.7	4020	5.4	142.1	.086	132.7	.177	4.69	.0028	29510	2.11
800[4]	7164	—	20944	26.2	3100	83110	47	11.5	4340	5.4	153.3	.087	138.6	.173	4.89	.0028	29590	2.17

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[1] The heat production was computed on the assumption that one liter of oxygen has a heat equivalent of 4.825 Cal.

[2] Surface area was computed from the equation, surface area in sq. meters = 0.1 (weight in kg.) 0.63. See Missouri Agr. Exp. Sta. Res. Bull. 115, p. 30.

[3] Computed on the assumption that one lb. *TDN* (total digestible nutrients) is equivalent to 1814 Cal. or 1 gm. of *TDN* to 4 Cal.

[4] Computations for these body weights are extrapolations beyond the range of actual data.

Table 14.4a. Energy Metabolism and Pulmonary Ventilation in Growing Swine.

Prediction Table for Ventilation Rate of Growing Swine for Both Sexes.[1]

Body Weight		Approximate Age (months)		Ventilation Rate (S.T.P.)					Ratio of oxygen consumption to ventilation rate $\% \frac{O_2 \text{ consumed}}{\text{Air inhaled}}$			
				Per minute				Per day				
				Liters		Cu ft		Liters per sq m	Duroc Jersey		Chester White	
Kg	Lb	M	F	Total	Per kg	Total	Per lb		M	F	M	F
5	11.0	1.5	1.5	3.36	.67	0.118	.0107	18007	1.65	1.65	1.65	1.65
10	22.0	3.3	3.0	5.20	.52	0.184	.0084	17970	1.87	2.00	1.87	2.00
15	33.1	4.3	4.0	6.72	.45	0.237	.0072	17967	2.07	2.17	2.07	2.17
20	44.1	5.0	4.7	8.05	.40	0.284	.0064	17941	2.24	2.42	2.24	2.42
25	55.1	5.3	5.1	9.27	.37	0.327	.0059	17937	2.40	2.55	2.40	2.55
50	110.2	7.3	6.6	14.35	.29	0.507	.0046	17906	2.90	3.05	2.90	3.05
75	165.3	9.4	8.3	18.52	.25	0.654	.0040	17875	2.17	2.36	2.40	2.36
100	220.5	11.0	10.0	22.20	.22	0.784	.0036	17859	2.19	2.16	2.50	2.35
125	275.6	13.0	11.5	25.55	.20	0.902	.0033	17852	2.17	2.01	2.58	2.34
150	330.7	14.5	13.5	28.66	.19	1.012	.0031	17843	2.18	1.89	2.64	2.30
175	385.8	18.0	15.5	31.59	.18	1.116	.0029	17839	2.18	1.80	2.70	2.31
200	440.9	21.0	18.0	34.36	.17	1.213	.0028	17830	2.16	1.74	2.75	2.28
225	496.0	23.0	22.0	37.01	.16	1.307	.0026	17824	2.18	1.67	2.78	2.29
250	551.1	25.0	25.0	39.55	.16	1.397	.0025	17820	2.16	1.62	2.83	2.28

Prediction Table for Resting Maintenance Energy Cost in Growing Chester White Swine for Both Sexes[1]

Body Weight		Approximate Age (mos)		Maintenance Energy Cost per 24 hours												Oxygen Consumption per 24 hours (S. T. P.)							
				Calories						B.T.U.				Equivalent[4] in TDN lbs		Liters				Cu ft			
				Total[2]		Per kg		Per sq m[3]		Total		Per lb				Total		Per kg		Total		Per lb	
Kg	Lb	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
5	11.0	1.5	1.5	386	386	77.2	77.2	1440	1440	1530	1530	139	139	0.2	0.2	80	80	16.0	16.0	2.8	2.8	.255	.255
10	22.0	3.3	3.0	676	724	67.6	72.4	1620	1740	2680	2870	122	130	0.4	0.4	140	150	14.0	15.0	4.9	5.3	.223	.241
15	33.1	4.3	4.0	965	1013	64.3	67.5	1790	1880	3830	4020	116	121	0.5	0.6	200	210	13.3	14.0	7.1	7.4	.214	.224
20	44.1	5.0	4.7	1254	1351	62.7	67.6	1940	2090	4980	5360	113	122	0.7	0.7	260	280	13.0	14.0	9.2	9.9	.209	.224
25	55.1	5.3	5.1	1544	1640	61.8	65.6	2070	2200	6130	6510	111	118	0.9	0.9	320	340	12.8	13.6	11.3	12.0	.205	.218
50	110.2	7.3	6.6	2895	3040	57.9	60.8	2510	2630	11490	12060	104	109	1.6	1.7	600	630	12.0	12.6	21.2	22.2	.192	.201
75	165.3	9.4	8.3	3088	3040	41.2	40.5	2070	2040	12250	12060	74	73	1.7	1.7	640	630	8.5	8.4	22.6	22.2	.137	.134
100	220.5	11.0	10.0	3860	3620	38.6	36.2	2160	2020	15320	14360	69	65	2.1	2.0	800	750	8.0	7.5	28.3	26.5	.128	.120
125	275.6	13.0	11.5	4584	4150	36.7	33.2	2220	2010	18190	16470	66	60	2.5	2.3	950	860	7.6	6.9	33.5	30.4	.122	.110
150	330.7	14.5	13.5	5259	4584	35.1	30.6	2270	1980	20870	18190	63	55	2.9	2.5	1090	950	7.3	6.3	38.5	33.5	.116	.101
175	385.8	18.0	15.5	5935	5066	33.9	28.9	2330	1990	23550	20100	61	52	3.3	2.8	1230	1050	7.0	6.0	43.4	37.1	.112	.096
200	440.9	21.0	18.0	6562	5452	32.8	27.3	2360	1960	26040	21630	59	49	3.6	3.0	1360	1130	6.8	5.6	48.0	39.9	.109	.090
225	496.0	23.0	22.0	7141	5886	31.7	26.2	2390	1970	28340	23360	57	47	3.9	3.2	1480	1220	6.6	5.4	52.3	43.1	.105	.087
250	551.1	25.0	25.0	7768	6272	31.1	25.1	2430	1960	30820	24890	56	45	4.3	3.5	1610	1300	6.4	5.2	56.9	45.9	.103	.083

Prediction Table for Resting Maintenance Energy Cost in Growing Duroc Jersey Swine for Both Sexes.[1]

Body Weight		Approximate Age (mos)		Maintenance Energy Cost per 24 hours														Oxygen Consumption per 24 hours (S. T. P.)							
				Calories						B.T.U.				Equivalent[4] in TDN lbs		Liters				Cu ft			
				Total[2]		Per kg		Per sq m[3]		Total		Per lb				Total		Per kg		Total		Per lb	
Kg	Lb	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
5	11.0	1.5	1.5	386	386	77.2	77.2	1440	1440	1530	1530	139	139	0.2	0.2	80	80	16.0	16.0	2.8	2.8	.255	.255
10	22.0	3.3	3.0	676	724	67.6	72.4	1620	1740	2680	2870	122	130	0.4	0.4	140	150	14.0	15.0	4.9	5.3	.223	.241
15	33.1	4.3	4.0	965	1013	64.3	67.5	1790	1880	3830	4020	116	121	0.5	0.6	200	210	13.3	14.0	7.1	7.4	.214	.224
20	44.1	5.0	4.7	1254	1351	62.7	67.6	1940	2090	4980	5360	113	122	0.7	0.7	260	280	13.0	14.0	9.2	9.9	.209	.224
25	55.1	5.3	5.1	1544	1640	61.8	65.6	2070	2210	6130	6510	111	118	0.9	0.9	320	340	12.8	13.6	11.3	12.0	.205	.218
50	110.2	7.3	6.6	2895	3040	57.9	60.8	2510	2630	11490	12060	104	109	1.6	1.7	600	630	12.0	12.6	21.2	22.2	.192	.201
75	165.3	9.4	8.3	2798	3040	37.3	40.5	1880	2040	11110	12060	67	73	1.5	1.7	580	630	7.7	8.4	20.4	22.2	.123	.134
100	220.5	11.0	10.0	3378	3330	33.8	33.3	1890	1860	13400	13210	61	60	1.9	1.8	700	690	7.0	6.9	24.7	24.4	.112	.111
125	275.6	13.0	11.5	3860	3570	30.0	28.6	1870	1732	15320	14170	56	51	2.1	2.0	800	740	6.4	5.9	28.3	26.1	.103	.095
150	330.7	14.5	13.5	4342	3764	28.9	25.1	1880	1627	17230	14940	52	45	2.4	2.1	900	780	6.0	5.2	31.8	27.5	.096	.083
175	385.8	18.0	15.5	4777	3956	27.3	22.6	1870	1551	18960	15700	49	41	2.6	2.2	990	820	5.7	4.7	35.0	29.0	.091	.075
200	440.9	21.0	18.0	5163	4150	25.8	20.8	1860	1500	20490	16470	46	37	2.8	2.3	1070	860	5.3	4.3	37.8	30.4	.086	.069
225	496.0	23.0	22.0	5597	4294	24.9	19.1	1870	1440	22210	17040	45	34	3.1	2.4	1160	890	5.2	4.0	41.0	31.4	.083	.063
250	551.1	25.0	25.0	5935	4439	23.7	17.8	1860	1390	23550	17610	43	32	3.3	2.4	1230	920	4.9	3.7	43.4	32.5	.079	.059

Prediction Table for 24-Hour Fasting Energy Metabolism in Growing Swine for Both Sexes.[1]

Body Weight		Approximate Age (mos)		Maintenance Energy Cost per 24 hours												Oxygen Consumption per 24 hours (S. T. P)							
				Calories						B.T.U.				Equivalent[4] in TDN lbs		Liters				Cu ft			
				Total[2]		Per kg		Per sq m[3]		Total		Per lb				Total		Per kg		Total		Per lb	
Kg	Lb	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
10	22.0	—	3.0	—	434	—	43.4	—	1040	—	1720	—	78	—	0.2	—	90	—	9.0	—	3.2	—	.145
15	33.1	4.3	4.0	627	579	41.8	38.6	1160	1080	2490	2300	75	69	0.3	0.3	130	120	8.7	8.0	4.6	4.2	.139	.127
20	44.1	5.0	4.7	820	772	41.0	38.6	1270	1190	3250	3060	74	69	0.4	0.4	170	160	8.5	8.0	6.0	5.7	.136	.129
25	55.1	5.3	5.1	965	917	38.6	36.7	1300	1230	3830	3640	70	66	0.5	0.5	200	190	8.0	7.6	7.1	6.7	.129	.122
50	110.2	7.3	6.6	1689	1592	33.8	31.8	1460	1380	6700	6320	61	57	0.9	0.9	350	330	7.0	6.6	12.4	11.7	.113	.106
75	165.3	9.4	8.3	2316	2268	30.9	30.2	1550	1520	9190	9000	56	54	1.3	1.2	480	470	6.4	6.3	17.0	16.6	.103	.100
100	220.5	11.0	10.0	2654	2316	26.5	23.2	1480	1290	10530	9190	48	42	1.5	1.3	550	480	5.5	4.8	19.4	17.0	.088	.077
125	275.6	13.0	11.5	2992	2606	23.9	20.8	1450	1260	11870	10340	43	38	1.6	1.4	620	540	5.0	4.3	21.9	19.1	.079	.069
150	330.7	14.5	13.5	3281	2798	21.9	18.7	1420	1210	13020	11100	39	34	1.8	1.5	680	580	4 5	3.9	24.0	20.5	.073	.062
175	385.8	18.0	15.5	3570	2992	20.4	17.1	1400	1170	14170	11870	37	31	2.0	1.6	740	620	4.2	3.5	26.1	21.9	.068	.057
200	440.9	21.0	18.0	3860	3184	19.3	15.9	1390	1150	15320	12630	35	29	2.1	1.8	800	660	4.0	3.3	28.3	23.3	.064	.053
225	496.0	23.0	22.0	4101	3378	18.2	15.0	1370	1130	16270	13400	33	27	2.3	1.9	850	700	3.8	3.1	30.0	24.7	.060	.050
250	551.1	25.0	25.0	4342	3522	17.4	14.1	1360	1100	17230	13980	31	25	2.4	1.9	900	730	3.6	2.9	31.8	25.8	.058	.047

[1] Males (M); females (F).

[2] The heat production was computed on the assumption that one liter of oxygen has a heat equivalent of 4.825 Calories.

[3] Surface area was computed from the equation, surface area in sq. meters = $0.097\ (\text{weight, kg})^{.633}$. See Missouri Agr. Exp. Sta. Res. Bull. 115, p. 30.

[4] Computed on the assumption that one lb. TDN (total digestible nutrients) is equivalent to 1814 Cal. or 1 gm. of TDN to 4 Cal.

For methods and equations for each set of data, consult Brody, S., and Kibler, H. H., "Energy metabolism and pulmonary ventilation in growing swine," Univ. Missouri Agr. Exp. Sta. Res. Bull. 380, 1944.

Table 14.5. "Basal Metabolism" Prediction Table for Man.

Ages	Body weight		S Area (sq. cm)	Metabolism, Cal/24 hrs.								Energy Metabolism Equivalents in Terms of Quantities* of Milk (4% Fat)			
				Males				Females				Males		Females	
	(kg)	(lb)		Total	Per kg.	Per lb.	Per sq. m.	Total	Per kg.	Per lb.	Per sq. m.	Quarts	Liters	Quarts	Liters
Birth to 3 yrs.	2	4.4	1585	105	53	24	662	104	52	24	656	0.14	0.136	0.14	0.135
	4	8.8	2593	212	53	24	818	215	54	24	829	0.29	0.274	0.29	0.278
	6	13.2	3449	321	54	24	931	329	55	25	954	0.44	0.415	0.45	0.426
	8	17.6	4217	430	54	24	1020	445	56	25	1055	0.59	0.556	0.61	0.576
	10	22.0	4925	540	54	25	1096	562	56	26	1141	0.74	0.699	0.77	0.727
	12	26.5	5588	650	54	25	1163	681	56	26	1219	0.89	0.841	0.93	0.881
	14	30.9	6216	760	54	25	1123	800	57	26	1287	1.0	0.983	1.1	1.035
	16	35.3	6814	871	54	25	1278	921	58	26	1352	1.2	1.127	1.3	1.191
3 to 16 yrs.	16	35.3	6814	760	48	22	1115	690	43	20	1013	1.0	1.0	0.95	0.9
	18	39.7	7389	815	45	21	1103	744	41	19	1007	1.1	1.1	1.0	1.0
	20	44.1	7942	867	43	20	1092	796	40	18	1002	1.2	1.2	1.1	1.0
	25	55.1	9250	989	40	18	1069	918	37	17	992	1.4	1.3	1.3	1.2
	30	66.1	10,470	1101	37	17	1052	1037	35	16	990	1.5	1.4	1.4	1.3
	35	77.2	11,630	1206	34	16	1037	1139	33	15	979	1.7	1.6	1.6	1.5
	40	88.2	12,720	1305	33	15	1026	1240	31	14	975	1.8	1.7	1.7	1.6
	45	99.2	13,780	1398	31	14	1015	1327	30	13	970	1.9	1.8	1.8	1.7
	50	110.2	14,790	1488	30	13	1006	1431	29	13	968	2.0	1.9	2.0	1.9
16 to 31 yrs.	40	88.2	12,720	1210	30	14	951	1168	29	13	918	1.7	1.6	1.6	1.5
	45	99.2	13,780	1306	29	13	948	1233	27	12	895	1.8	1.7	1.7	1.6
	50	110.2	14,790	1399	28	13	946	1294	26	12	875	1.9	1.8	1.8	1.7
	55	121.3	15,770	1488	27	12	944	1352	25	11	857	2.0	1.9	1.9	1.7
	60	132.3	16,710	1575	26	12	943	1407	23	11	842	2.2	2.0	1.9	1.8
	65	143.3	17,630	1658	26	12	941	1460	22	10	828	2.3	2.1	2.0	1.9
	70	154.3	18,530	1741	25	11	940	1510	22	10	815	2.4	2.3	2.1	2.0
	75	165.3	19,400	1821	24	11	939	1559	21	9	804	2.5	2.4	2.1	2.0
	80	176.4	20,260	1898	24	11	937	1606	20	9	793	2.6	2.5	2.2	2.1
	85	187.4	21,090	1974	23	11	936	1652	19	9	783	2.7	2.6	2.3	2.1
	90	198.4	21,910	2049	23	10	935	1696	19	9	774	2.8	2.7	2.3	2.2
	95	209.4	22,710	2122	22	10	934	1738	18	8	765	2.9	2.7	2.4	2.2
	100	220.5	23,490	2194	22	10	934	1780	18	8	758	3.0	2.8	2.4	2.3

* 1 qt. of milk = 2.15 lb. (20° C.) = 730 Calories; 1 liter of milk = 1.031 kg = 773 Calories.

Table 14.5. (cont'd) "Basal Metabolism" Prediction Table for Man.

Ages	Body Weight		S Area (sq. cm.)	Metabolism, Cal/24 hrs.								Energy Metabolism Equivalents in Terms of Quantities* of Milk (4% Fat)			
				Males				Females				Males		Females	
	(kg)	(lb)		Total	Per kg.	Per lb.	Per sq. m.	Total	Per kg.	Per lb.	Per sq. m.	Quarts	Liters	Quarts	Liters
31 to 60 yrs.	35	77.2	11,640	1091	31	14	938	1089	31	14	936	1.5	1.4	1.5	1.4
	40	88.2	12,720	1176	29	13	925	1146	29	13	901	1.6	1.5	1.6	1.5
	45	99.2	13,780	1256	28	13	911	1198	27	12	869	1.7	1.6	1.6	1.5
	50	110.2	14,790	1332	27	12	901	1247	25	11	843	1.8	1.7	1.7	1.6
	55	121.3	15,770	1405	26	12	891	1293	24	11	820	1.9	1.8	1.8	1.7
	60	132.3	16,710	1475	25	11	883	1336	22	10	800	2.0	1.9	1.8	1.7
	65	143.3	17,630	1543	24	11	875	1378	21	10	782	2.1	2.0	1.9	1.8
	70	154.3	18,530	1608	23	10	868	1417	20	9	765	2.2	2.1	1.9	1.8
	75	165.3	19,400	1672	22	10	862	1454	19	9	749	2.3	2.2	2.0	1.9
	80	176.4	20,260	1733	22	10	855	1490	19	8	735	2.4	2.2	2.0	1.9
	85	187.4	21,090	1793	21	10	850	1525	18	8	723	2.5	2.3	2.1	2.0
	90	198.4	21,910	1851	21	9	845	1559	17	8	712	2.5	2.4	2.1	2.0
	95	209.4	22,710	1909	20	9	841	1591	17	8	701	2.6	2.5	2.2	2.1
	100	220.5	23,490	1964	20	9	836	1623	16	7	691	2.7	2.5	2.2	2.1
over 60 yrs.	45	99.2	13,780	1160	26	12	842	1060	24	11	769	1.6	1.5	1.5	1.4
	50	110.2	14,790	1230	25	11	832	1125	23	10	761	1.7	1.6	1.5	1.5
	55	121.3	15,770	1296	24	11	822	1188	22	10	753	1.8	1.7	1.6	1.5
	60	132.3	16,710	1359	23	10	813	1248	21	9	747	1.9	1.8	1.7	1.6
	65	143.3	17,630	1420	22	10	805	1306	20	9	741	1.9	1.8	1.8	1.7
	70	154.3	18,530	1479	21	10	798	1363	19	9	736	2.0	1.9	1.9	1.8
	75	165.3	19,400	1537	20	9	792	1418	19	9	731	2.1	2.0	1.9	1.8
	80	176.4	20,260	1592	20	9	786	1471	18	8	726	2.2	2.1	2.0	1.9
	85	187.4	21,090	1646	19	9	780	1522	18	8	722	2.3	2.1	2.1	2.0
	90	198.4	21,910	1699	19	9	775	1573	17	8	718	2.3	2.2	2.2	2.0
	95	209.4	22,710	1750	18	8	771	1622	17	8	714	2.4	2.3	2.2	2.1
	100	220.5	23,490	1800	18	8	766	1670	17	8	711	2.5	2.3	2.3	2.2

* 1 qt. of milk = 2.15 lb. (20° C.) = 730 Calories; 1 liter of milk = 1.031 kg = 773 Calories.

Table 14.6. Data on the Relation between Heat Increment of Gestation and Birth Weight of Offspring

Species & Breed	No. of Animals in Average	Weight of newborn Individual or litter (kgs.)	Estimated Surface Area of newborn (sq. meters)	Mother's Wt. gain during pregnancy (kg.)	Heat Increment of Gestation		Gestation Period (days)	No. in Litter	Source
					Total Cal.	Cal./kg. Birth Wt.			
Percheron horse	1	74.0	1.505	113	591,000	7986	340	1	Original
Holstein cows	16	40.8	1.197	94	353,400	8662	283	1	"
Hereford cows	3	31.8	1.040	45	304,500	9575	283	1	"
Jersey cows	18	25.4	.918	44	228,300	8988	283	1	"
Duroc-Jersey swine	6	6.5	—	9	42,120	6480	114	..	"
Duroc-Jersey swine	1	8.1	.....	10	65,520	8089	114	7	"
Duroc-Jersey swine	1	4.3	.....	.....	25,500	5930	114	3	"
Duroc-Jersey swine	1	2.7	.....	6	9,200	3407	114	2	"
Dorset sheep	1	5.0	.300	6	23,800	4755	150	1	"
Dorset sheep	1	3.7	.251	5.5	21,600	5838	150	1	"
Human	1	3.8	.251	8.3	22,540	5932	280	1	Root and Root
Human	1	3.6	.242	7.7	21,805	6057	280	1	Sandiford and Wheeler
Goat	1	7.7	.455	1.5	53,300	6922	150	2	Original
Goat	1	3.2*	.203	−1.8	37,300	11660	150	1	"
Goat	1	5.2*	.347	3.2	57,800	11120	150	2	"
Rat	1	0.0225	.....	.....	38.7	1724	21	5	Original
Rat	1	0.0135	.....	.....	38.8	2874	21	3	"
Rat	1	0.058	.....	0.016	88.3	1522	21	12	"
Rat	1	0.050	.....	0.014	57.0	1140	21	9	"
Rat	1	0.059	.....	0.024	94.8	1607	21	13	"
Rat	1	0.052	.....	0.026	84.8	1631	21	12	"
Domestic fowl†		....	.116	.....	19	501	21	..	Average various sources

* Estimated on basis of average values.

† Omitted from correlation.

Table 14.7. Live Weight, Resting and Basal Metabolism of Jersey Cattle, Females, at Different Ages

Age (mos)	Live Weight (kg)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
2	44.0	48.2	36.5	2121	1606
4	73.0	42.6	32.2	3110	2351
6	111	37.9	28.7	4207	3186
8	146	34.1	25.8	4979	3767
10	174	30.9	23.4	5377	4072
12	201	28.4	21.5	5708	4322
14	228	26.2	19.8	5974	4514
16	256	24.3	18.4	6221	4710
18	283	22.9	17.3	6481	4896
20	310	21.7	16.4	6727	5084
22	338	20.7	15.7	6997	5307
24	366	19.9	15.1	7283	5527
26	396	19.2	14.5	7603	5742
28	404	18.7	14.2	7555	5737
30	404	18.2	13.8	7353	5575
32	406	17.8	13.5	7227	5481
34	416	17.5	13.2	7280	5491
36	434	17.2	13.0	7465	5642
38	456	17.0	12.9	7752	5882
40	480	16.8	12.7	8064	6096

$$Q/m = 39e^{-.096t} + 16$$
$$Qb/m = Q/m - (Q/m \times 0.243)$$

Q/m is *resting* metabolism per unit body weight; Qb/m is *basal* metabolism per unit body weight, m.

Table 14.8. Live Weight, Resting and Basal Metabolism of Jersey Cattle, Males, at Different Ages

Age (mos)	Live Weight (kgs)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
2	47	48.8	36.1	2294	1697
4	80	43.0	31.8	3440	2544
6	120	38.3	28.3	4596	3396
8	155	34.4	25.5	5332	3953
10	193	31.3	23.2	6041	4478
12	232	28.8	21.3	6682	4942
14	270	26.7	19.8	7209	5346
16	310	25.1	18.6	7781	5766
18	345	23.7	17.5	8177	6038
20	377	22.6	16.7	8520	6296
22	410	21.8	16.1	8938	6601
24	435	21.0	15.5	9135	6743

$$Q/m = 38e^{-.105t} + 18$$
$$Qb/m = 28.1e^{-.105t} + 13.3$$

Table 14.9. Live Weight, Resting and Basal Metabolism of Holstein Cattle, Females, at Different Ages

Age (mos)	Live Weight (kg)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
2	62	41.0	31.6	2542	1959
4	100	36.9	28.4	3690	2840
6	145	33.3	25.7	4829	3727
8	186	30.4	23.4	5654	4352
10	221	27.8	21.4	6144	4729
12	255	25.6	19.7	6528	5024
14	292	23.8	18.3	6950	5344
16	330	22.4	17.3	7392	5709
18	367	21.1	16.3	7744	5982
20	403	20.0	15.4	8060	6206
22	440	19.0	14.6	8360	6424
24	483	18.3	14.1	8839	6810
26	524	17.6	13.6	9222	7126
28	544	17.0	13.1	9248	7126
30	509	16.6	12.8	8449	6515
32	490	16.2	12.5	7938	6125
34	508	15.8	12.2	8026	6198
36	520	15.6	12.0	8112	6240
38	536	15.3	11.8	8201	6325
40	553	15.1	11.6	8350	6415

$$Q/m = 32e^{-.084t} + 14$$
$$Qb/m = Q/m - (Q/m \times 0.229)$$

Table 14.10. Live Weight, Resting and Basal Metabolism of Sheep, Females, at Different Ages

Age (mos)	Live Weight (kg)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
2	18.5	55.3	44.9	1023	831
4	33.5	45.3	36.8	1518	1233
6	39.8	38.7	31.5	1540	1254
8	44.1	34.6	28.1	1526	1239
10	48.0	31.8	25.9	1526	1243
12	53.3	30.1	24.5	1604	1306
14	59.7	29.0	23.6	1731	1409
16	53.0	28.3	23.1	1500	1224
18	54.6	27.8	22.7	1518	1239
20	55.8	27.5	22.4	1535	1250
22	60.8	27.4	22.3	1666	1356
24	64.7	27.2	22.2	1760	1436
26	59.7	27.1	22.1	1618	1319
28	56.7	27.1	22.1	1537	1253
30	58.5	27.0	22.0	1580	1287

$$Q/m = 44e^{-.22t} + 27$$
$$Qb/m = 35.6e^{-.22t} + 22$$

Table 14.11. Live Weight, Resting and Basal Metabolism of Sheep, Wethers, at Different Ages

Age (mos)	Live Weight (kg)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
2	18.5	——	33.2	——	614
4	34.0	46.6	30.8	1584	1047
6	41.2	43.2	28.7	1780	1182
8	45.8	40.1	26.8	1837	1227
10	51.0	37.4	25.1	1907	1280
12	58.3	35.1	23.7	2046	1382
14	65.0	33.0	22.4	2145	1456
16	69.7	31.1	21.3	2168	1485
18	74.0	29.5	20.3	2183	1502
20	78.2	28.0	19.4	2190	1517
22	83.1	26.7	18.6	2219	1546
24	87.7	25.6	17.9	2245	1570
26	89.7	24.6	17.4	2207	1561
28	84.9	23.7	16.8	2012	1426
30	90.9	22.9	16.4	2082	1491

$$Q/m = 38e^{-.062t} + 17$$
$$Qb/m = 23e^{-.064t} + 13$$

Table 14.12. Live Weight, Resting and Basal Metabolism of Beef Cattle, Females, at Different Ages

Age (mos)	Live Weight (kg)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
4	87	40.1	23.7	3489	2062
6	130	35.4	22.1	4602	2873
8	174	31.5	20.8	5481	3619
10	214	28.4	19.6	6078	4194
12	247	25.7	18.7	6348	4619
14	280	23.6	17.9	6608	5012
16	317	21.9	17.3	6942	5484
18	351	20.4	16.7	7160	5862
20	383	19.3	16.3	7392	6243
22	399	18.3	15.9	7302	6344
24	416	17.5	15.6	7280	6490
26	452	16.9	15.3	7639	6916
28	444	16.3	15.1	7237	6704
30	417	16.0	14.9	6672	6213
32	414	15.6	14.8	6458	6127
34	423	15.3	14.6	6472	6176
36	435	15.1	14.5	6569	6308
38	450	14.9	14.4	6705	6480
40	454	14.7	14.4	6674	6538
42	456	14.6	14.3	6658	6521

$$Q/m = 39e^{-.10t} + 14$$
$$Qb/m = 14e^{-.091t} + 14$$

Table 14.13. Live Weight, Resting and Basal Metabolism of Beef Steers at Different Ages

Age (mos)	Live Weight (kg)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
4	116	36.3	27.6	4211	3203
6	172	32.1	24.4	5521	4197
8	228	28.7	21.8	6544	4970
10	280	26.0	19.8	7280	5544
12	336	23.8	18.1	7997	6082
14	384	22.1	16.8	8486	6451
16	433	20.7	15.8	8963	6841
18	483	19.6	15.0	9467	7245
20	530	18.7	14.3	9911	7579
22	575	17.9	13.7	10293	7878
24	622	17.1	13.2	10761	8210
26	665	16.9	12.9	11239	8579
28	706	16.5	12.6	11649	8896
30	745	16.2	12.4	12069	9238
32	781	16.0	12.2	12496	9528
34	810	15.8	12.1	12798	9801
36	840	15.6	11.9	13104	9996
38	865	15.5	11.8	13408	10207
40	888	15.4	11.8	13675	10478

$$Q/m = 33e^{-.11t} + 15$$
$$Qb/m = 25e^{-.11t} + 11.5$$

Table 14.14 Live Weight, Resting and Basal Metabolism of Horses, Females and Geldings Combined, at Different Ages

Age (mos)	Live Weight (kg)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
2	166	37.9	28.7	6291	4764
4	247	30.7	25.9	7583	6397
6	297	26.8	23.6	7960	7009
8	336	24.6	21.7	8266	7291
10	369	23.5	20.2	8672	7454
12	400	22.8	18.9	9120	7560
14	426	22.4	17.9	9542	7625
16	446	22.2	17.0	9901	7582
18	457	22.1	16.3	10100	7449
20	469	22.1	15.7	10365	7363
22	482	22.0	15.2	10604	7326
24	507	22.0	14.8	11154	7504
26	544	22.0	14.5	11968	7888
28	576	22.0	14.3	12672	8237
30	607	22.0	14.0	13354	8498
32	632	22.0	13.9	13904	8785
34	660	22.0	13.7	14520	9042
36	649	22.0	13.6	14278	8826
38	635	22.0	13.5	13970	8573
40	658	22.0	13.4	14476	8817

$$Q/m = 29e^{-.30t} + 22$$
$$Qb/m = 19e^{-.097t} + 13$$

Table 14.15 Live Weight, Resting and Basal Metabolism of Swine, Females, at Different Ages

Age (mos)	Live Weight (kg)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
2	8.0	118.1	48.6	945	389
4	23	80.6	37.3	1853	858
6	55	57.1	29.6	3141	1628
8	94	42.1	24.4	3957	2294
10	126	32.6	20.7	4108	2608
12	152	26.6	18.3	4043	2782
14	173	22.9	16.6	3962	2872
16	194	20.5	15.5	3977	3007
18	213	19.1	14.7	4068	3131
20	227	18.1	14.1	4109	3201
22	240	17.5	13.8	4200	3312
24	252	17.1	13.5	4309	3402
26	260	17.0	13.4	4420	3484
28	266	16.8	13.3	4469	3538
30	269	16.7	13.2	4492	3551
32	270	16.5	13.1	4455	3537
34	270	16.5	13.0	4455	3510
36	270	16.5	13.0	4455	3510

$$Q/m = 161e^{-.23t} + 16.5$$
$$Qb/m = 52e^{-.19t} + 13$$

Table 14.16 Live Weight, Resting and Basal Metabolism of Swine, Males, at Different Ages

Age (mos)	Live Weight (kg)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
2	7	86.0	50.8	602	356
4	20	66.7	39.6	1334	792
6	47	53.0	32.2	2491	1513
8	74	43.5	27.3	3219	2020
10	98	36.7	24.1	3597	2362
12	118	31.8	22.0	3752	2596
14	139	28.5	20.6	3962	2863
16	159	26.2	19.7	4166	3132
18	177	24.5	19.1	4337	3381
20	195	23.3	18.8	4544	3666
22	212	22.4	18.5	4749	3922
24	228	21.9	18.3	4993	4172
26	244	21.5	18.2	5246	4441
28	258	21.1	18.2	5444	4696
30	273	21.0	18.1	5733	4941

$$Q/m = 93e^{-.176t} + 20.5$$
$$Qb/m = 50e^{-.21t} + 18$$

Table 14.17 Live Weight, Resting and Basal Metabolism of Deighton's[1] Swine at Different Ages

Age (mos)	Live Weight (kg)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
				223	
2	12	75.1	—	901	—
4	24	61.4	34.8	1474	835
6	42	50.7	30.6	2129	1285
8	60	42.5	27.1	2550	1626
10	78	36.3	24.2	2831	1888
12	96	31.4	21.7	3014	2083
14	114	27.6	19.8	3146	2257
16	131	24.8	18.1	3249	2371
18	149	22.5	16.8	3353	2503
20	164	20.8	15.6	3411	2558
22	177	19.4	14.6	3434	2584
24	189	18.4	13.9	3478	2627
26	200	17.7	13.2	3540	2640
28	211	17.0	—	3587	—
30	220	16.6	—	3652	—

$$Q/m = 78e^{-.13t} + 15$$
$$Qb/m = 36e^{-.093t} + 10$$

[1] Deighton, T. A., *J. Agr. Sci.*, **19**, 140 (1929).

Table 14.18 Resting Metabolism, Basal Metabolism, and Heat Increment of Feeding in Horses for different weights

Weight (kg)	Heat Production in Calories per Day											
	Resting Metabolism				Basal Metabolism				Heat Increment of Feeding			
	Full Fed[1]	Half Fed[2]	Female[3]	Geldings[4]	Full Fed	Half Fed	Female	Geldings	Full Fed	Half Fed	Female	Geldings
300	7920	7740	8160	8190	5481	5031	5949	5332	2439	2709	2211	2858
325	8353	8125	8548	8515	5780	5281	6231	5543	2573	2844	2317	2972
350	8750	8540	8925	8855	6055	5551	6506	5765	2695	2989	2419	3090
375	9225	9000	9338	9225	6384	5850	6807	6005	2841	3150	2531	3220
400	9720	9440	9720	9600	6726	6136	7086	6250	2994	3304	2634	3350
425	10200	9903	10158	9988	7058	6437	7405	6502	3142	3466	2753	3486
450	10710	10350	10575	10350	7411	6727	7709	6738	3299	3623	2866	3612
475	11210	10830	11020	10783	7757	7039	8034	7020	3453	3791	2986	3763
500	11700	11300	11500	11206	8096	7345	8383	7291	3604	3955	3117	3909
525	12285	11813	11970	11603	8501	7678	8726	7554	3784	4135	3244	4049
550	12815	12320	12430	12100	8868	8008	9061	7877	3947	4312	3369	4223
575	13340	12823	12880	12535	9231	8335	9390	8160	4109	4488	3490	4375
600	13860	13380	13380	13020	9591	8697	9754	8476	4269	4683	3626	4544
625	14438	13875	13875	13438	9991	9019	10115	8748	4447	4856	3760	4690
650	15015	14430	14365	13975	10390	9379	10472	9098	4625	5051	3893	4877
675	15593	14985	14850	14445	10790	9740	10826	9404	4803	5245	4024	5041
700	16170	15470	15400	14910	11190	10055	11227	9706	4980	5415	4173	5204

[1] $Q/m = 70e^{-.0101m} + 23$

[2] $Q/m = 53e^{-.0088m} + 22$

[3] $Q/m = 49e^{-.0078m} + 21.7$

[4] $Q/m = 60e^{-.0078m} + 21$

Table 14.19 Live Weight, Resting and Basal Metabolism of Holstein Cattle, Males, at Different Ages

Age (mos)	Live Weight (kg)	Metabolism (Cal/kg/day)		Metabolism (Cal/day)	
		Resting	Basal	Resting	Basal
2	71	42.9	—	3046	—
4	112	37.6	—	4211	—
6	166	33.0	—	5478	—
8	226	28.9	—	6531	—
10	280	25.3	—	7084	—
12	333	22.2	—	7393	—
14	380	19.5	—	7410	—

$$Q/m = 49e^{-.066t}$$

Table 14.20 Resting Metabolism, Basal Metabolism, and Heat Increment of Feeding in Dairy Cattle for different weights

Wt. (kg)	Heat Production in Calories per Day														
	Resting Metabolism					Basal Metabolism					Heat Increment of Feeding				
	Hols. Fems. 1	Jersey Fems. 2	Under-fed Jersey Fems. 3	Jersey Steer & Free-Martin 4	Jersey Males 5	Hols. Fems. 1a	Jersey Fems. 2a	Under-fed Jersey Fems. 3a	Jersey Steer & Free-Martin 4a	Jersey Males 5a	Hols. Fems.	Jersey Fems.	Under-fed Jersey Fems.	Jersey Steer & Free-Martin	Jersey Males
25	1175	1355	1368	1255	1270	897	1007	1045	917	932	278	348	323	338	338
50	2190	2420	2390	2325	2350	1671	1798	1826	1700	1725	519	622	564	625	625
75	3050	3260	3173	3233	3270	2327	2422	2424	2363	2400	723	838	749	870	870
100	3800	3900	3770	4010	4060	2899	2898	2880	2931	2980	901	1002	890	1079	1080
125	4435	4460	4238	4663	4750	3384	3314	3238	3409	3486	1051	1146	1000	1254	1264
150	4995	4905	4620	5220	5340	3811	3644	3530	3816	3920	1184	1261	1090	1404	1420
175	5495	5285	4970	5688	5845	4193	3927	3797	4158	4290	1302	1358	1173	1530	1555
200	5940	5600	5260	6100	6320	4532	4161	4019	4459	4639	1408	1439	1241	1641	1681
225	6320	5895	5535	6435	6705	4822	4380	4229	4704	4921	1498	1515	1306	1731	1784
250	6675	6150	5800	6725	7100	5093	4569	4431	4916	5211	1582	1581	1369	1809	1889
275	6985	6410	6078	6958	7425	5330	4763	4644	5086	5450	1655	1647	1434	1872	1975
300	7290	6660	6360	7170	7740	5562	4948	4859	5241	5681	1728	1712	1501	1929	2059
325	7605	6923	6630	7378	8027	5803	5144	5065	5393	5892	1802	1779	1565	1985	2135
350	7860	7175	6930	7525	8330	5997	5331	5295	5501	6114	1863	1844	1635	1024	2216
375	8138	7425	7238	7688	8588	6209	5517	5530	5620	6304	1929	1908	1708	2068	2284
400	8360	7680	7560	7800	8880	6379	5706	5776	5702	6518	1981	1974	1784	2098	2362
425	8628	7948	7863	7948	9138	6583	5905	6007	5810	6707	2045	2043	1856	2138	2431
450	8910	8235	8190	8055	9405	6801	6119	6257	5888	6903	2109	2116	1933	2167	2502
475	9120	8550	8550	8170	9690	6959	6353	6532	5972	7112	2161	2197	2018	2198	2578
500	9450	8850	8900	8250	9950	7210	6576	6800	6031	7303	2240	2274	2100	2219	2647

1. $Q/m = 36e^{-.0045m} + 15$
2. $Q/m = 45e^{-.0066m} + 16$
3. $Q/m = 35e^{-.008m} + 17$
4. $Q/m = 44e^{-.0039m} + 10.3$
5. $Q/m = 39e^{-.0046m} + 16$

1a. $Qb/m = 28e^{-.0045m} + 11.4$
2a. $Qb/m = 33e^{-.0066m} + 12$
3a. $Qb/m = 35e^{-.008m} + 13$
4a. $Qb/m = 32e^{-.0039m} + 7.3$
5a. $Qb/m = 29e^{-.0046m} + 11.7$

Table 14.21 Resting Metabolism, Basal Metabolism, and Heat Increment of Feeding in Beef Cattle for different weights

Weight (kg)	Heat Production in Calories per Day					
	Resting Metabolism		Basal Metabolism		Heat Increment of Feeding	
	Females[1]	Steers[2]	Females[1a]	Steers[2a]	Females	Steers
25	1505	1155	765	855	740	300
50	2675	2140	1420	1584	1255	556
75	3585	2980	1995	2205	1590	775
100	4290	3700	2480	2738	1810	962
125	4825	4340	2913	3212	1912	1128
150	5265	4890	3300	3619	1965	1271
175	5580	5370	3640	3974	1940	1396
200	5840	5800	3940	4292	1900	1508
225	6050	6210	4230	4595	1820	1615
250	6250	6550	4475	4847	1775	1703
275	6410	6900	4730	5106	1680	1794
300	6540	7230	4950	5350	1590	1880
325	6695	7508	5168	5556	1527	1952
350	6825	7805	5390	5776	1435	2029
375	6975	8100	5588	5994	1387	2106
400	7120	8400	5800	6216	1320	2184
425	7268	8670	5993	6416	1275	2254
450	7425	8955	6165	6627	1260	2328
475	7600	9263	6365	6855	1235	2408
500	7800	9550	6600	7067	1200	2483
525	—	9818	—	7265	—	2553
550	—	10120	—	7489	—	2631
575	—	10408	—	7702	—	2706
600	—	10740	—	7948	—	2792
625	—	11063	—	8187	—	2876
650	—	11375	—	8417	—	2958
675	—	11678	—	8642	—	3036
700	—	12040	—	8910	—	3130

[1] $Q/m = 55e^{-.0061m} + 13$ [1a] $Qb/m = 22e^{-.0046m} + 11$

[2] $Q/m = 34e^{-.0048m} + 16$ [2a] $Qb/m = 25e^{-.0048m} + 12$

Table 14.22 Resting Metabolism, Basal Metabolism, and Heat Increment of Feeding in Sheep for different weights

Weight (kg)	Heat Production in Calories per Day					
	Resting Metabolism		Basal Metabolism		Heat Increment of Feeding	
	Females[1]	Wethers[2]	Females	Wethers[2a]	Females	Wethers
25	1240	1340	856	943	384	397
50	1575	1865	1087	1313	488	552
75	1740	2090	1201	1471	539	619
100	1930	2240	1332	1577	598	663

[1] $Q/m = 73e^{-.031m} + 16$

[2] $Q/m = 67e^{-.022m} + 15$ [2a] $Qb/m = 47e^{-.022m} + 10.6$

Table 14.23 Resting Metabolism, Basal Metabolism, and Heat Increment of Feeding in Swine for different weights

Wt. (kg)	Heat Production in Calories per Day								
	Resting Metabolism			Basal Metabolism			Heat Increment of Feeding		
	Females[1]	Males[2]	Deighton's[3]	Females[1a]	Males[2a]	Deighton's[3a]	Females	Males	Deighton's
25	1680	1610	1548	905	993	1130	775	617	418
50	2620	2565	2380	1440	1605	1480	1180	960	900
75	3130	3140	2813	1770	2033	1868	1360	1107	945
100	3400	3530	3030	2010	2370	2130	1390	1160	900
125	3550	3810	3163	2200	2688	2325	1350	1122	834
150	3660	4080	3255	2385	3000	2475	1275	1080	780
175	3760	4340	3360	2573	3325	2625	1187	1015	735
200	3880	4640	3500	2780	3660	2760	1100	980	740
225	4005	4930	3668	2993	4028	2903	1012	902	765
250	4200	5250	3850	3225	4400	3050	975	850	800
275	4400	—	4070	3465	—	3218	935	—	852
300	4650	—	4290	3720	—	3390	930	—	900
325	—	—	4550	—	—	3575	—	—	975
350	—	—	4830	—	—	3745	—	—	1085

[1] $Q/m = 74e^{-.0131m} + 14$

[2] $Q/m = 64e^{-.0137m} + 19$

[3] $Q/m = 69e^{-.014m} + 13.3$

[1a] $Qb/m = 35e^{-.0147m} + 12$

[2a] $Qb/m = 34e^{-.0162m} + 17$

[3a] $Qb/m = 34e^{-.011m} + 10$

Chapter 15

Maintenance Needs in Relation to Basal Metabolism, Body Size, and Productive Efficiency

> It has been estimated that the . . . maintenance requirement is between 11 and 15 per cent above the starvation minimum. *Graham Lusk*

The energy cost of maintenance is the *net* dietary energy (Ch. 2) required to keep the organism in a "steady" energetic state—the net dietary energy required to replace the energy expended while carrying on "maintenance" life processes. Maintenance life is conventionally differentiated from productive life in that maintenance living does not involve the production of milk, eggs, wool, flesh, etc., or muscular work aside from that associated with carrying out the normal non-productive life processes.

The major maintenance-energy expense is the basal energy metabolism. According to the quotation at the head of this chapter, the basal metabolism is approximately 85 per cent of the maintenance energy metabolism.

The second largest expense for maintenance is the muscular expense, for example, the walking about associated with living. Now the expense of walking and similar muscular exertion is proportional to body weight, $W^{1.0}$ (Ch. 24), not to $W^{0.7}$, as is the case for basal or resting metabolism (Chs. 13, 14). However, reasoning on the basis of dimensional analysis (Chs. 10 and 17) leads to the conclusion that the larger the animal the slower and the fewer the movements, so that the voluntary energy expenditure for muscular exercise tends to parallel the basal metabolism, *i.e.*, it tends to vary with $W^{0.7}$ rather than with $W^{1.0}$.

By similar dimensional-analytic reasoning one may generalize that what is true of voluntary muscular work is true of all productive processes: other conditions being equal, the maximal, or limiting, productive capacity tends to vary with basal energy metabolism—with approximately $W^{0.7}$—rather than with $W^{1.0}$. Kleiber[1] observed that the maximal relative food capacity, that is, the maximal value of the ratio $\dfrac{\text{maximal food energy consumption}}{\text{basal energy metabolism}}$ is approximately 5 in such diversely sized animals as cattle, rabbits, and chickens; from this he concluded that, other conditions being equal, productive efficiency is independent of body size[2].

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[1] Kleiber, M., *Die Tierwelt*, **36**, 437 (1926); *Tierernahrung*, **5**, 1 (1933).

[2] For a review of Kleiber's work, see Brody, S., *Ann. Rev. Biochem.*, **4**, 383 (1935).

Here is how Crasemann[3] exemplifies the idea by carrying out the computation on milk production of one 800-kg and of two 400-kg dairy cows.

	Total weight (kg)	Fasting metabolism (Cal/day)	Maintenance metabolizable energy cost, 1.67 times fasting (Cal/day)	Maximal metabolizable energy ingestion, 5 times basal (Cal/day)	Metabolizable energy above maintenance (Cal/day)	Milk production (Cal/day)	Conversion of metabolizable energy into milk energy (%)	Conversion of metabolizable energy above maintenance into milk energy (%)
One 800-kg cow	800	7800	13000	39000	26000	19500	50	75
Two 400-kg cows	800	9800	16400	49000	32000	24500	50	75

The efficiency of milk production is here independent of body size, and the same is probably true of other productive processes (Chs. 3 and 22), including maintenance, which is in a special category (static) of a productive process.

The foregoing discussion represents the writer's ideas which, however, are not generally accepted, as indicated by the following discussion.

In reply to the question concerning the relation of maintenance to basal energy needs, F. G. Benedict replied as follows:

"Basal metabolism is one thing. Energy-food requirements for maintenance is quite a different thing . . . I find myself quite unwilling to make any definite statement."

E. B. Forbes ended his reply to the same question by saying that "when a fish bites on a bare hook, he is indeed a poor fish", and so decided to "stick rather close to experimental evidence", and there is no experimental evidence for generalizing at this time.

H. H. Mitchell replied that the voluntary "activity increment", one of the major factors in the energy expense of maintenance, probably does not vary with the same function of body weight as does basal metabolism. However, he felt "no particular hesitation in saying that the maintenance requirement of protein, expressed in terms of body expenditures of nitrogen, will vary for adult animals with a power function of body weight", probably to the same degree as basal energy does.

The activity increment with respect to basal metabolism was reported to be 50 to 75 per cent in humans under sedentary occupation[4]; 50 per cent in poultry[5]; about 20 per cent in swine[6]; very slight in rats[7] and cattle. Armsby[8] computed the net energy of beef cattle maintained at constant weight in the feed lot to be approximately the same as the estimated heat production of fasting cattle in the respiration chamber. These species differences do not seem reasonable to the present reviewer and are probably due to differences in experimental methods.

In reply to this question J. R. Murlin described an elaborate experiment, as yet unpublished, which (said Murlin) "makes me believe emphatically in the idea that energy requirement for maintenance under ordinary living conditions is definitely related to body surface, or, if you prefer to put it that way, to some fractional power of the body weight."

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[3] Crasemann, von Edgar, "Mitteilungen aus dem Giebiete Lebensmitteluntersuchung und Hygiene," *Eidg. Gesundheitsaml in Bern*, **33,** Heft 3/4 (1942).

[4] Orr, J. B., and Leitch, I., *Nut. Abst. and Rev.*, **7,** 509 (1937–8).

[5] Mitchell, H. H., Card, L. E., and Hamilton, T. S., Univ. Ill. Agr. Exp. Sta. Bull. 367, 1931 (Table 41, pp. 132–3).

[6] Mitchell, H. H., and Kelley, M. A. R., *J. Agr. Res.*, **56,** 811 (1938).

[7] Mitchell, H. H., and Carman, G. G., *Am. J. Physiol.*, **76,** 409 Table 8 (1926).

[8] Armsby, H. P., "Nutrition of farm animals", New York, p. 291, 1917.

Livestock feeders usually allow so much maintenance per 100 or per 1000 lbs live weight. Thus for maintenance of dairy cattle Haecker[9], Morrison[10] (old standard), Savage[11], and Gaines[12] allow 8.0 lbs *TDN* per 1000 lbs live weight. Eckles[13] 7.5; Kellner[14] 6.7; Armsby[14] 6.5; Forbes and Kriss[14] 6.0; Möllgaard[14] 5.9; Hannsson[14] 5.7 lbs *TDN* per 1000 lbs live weight. No allowance was made in the ratio of *TDN* per 1000 lbs live weight for small and large cows, under the tacit assumption that, unlike basal metabolism, the maintenance energy cost varies directly with simple body weight, not with $W^{0.7}$

On the other hand while, *e.g.*, 120-lb sheep or goats are generally thought by practical livestock feeders to need 2 lbs *TDN*/day for maintenance, 1200-lb cattle are usually thought to need not 20 but only 10 lbs *TDN*/day for maintenance, which turns out to vary in proportion not to $W^{1.0}$ but approximately to $W^{0.7}$ ($TDN = 0.0704W^{0.699}$). In the 1936 edition of Morrison's "Feeds and Feeding", the maintenance standard for horses is given to vary with the 0.73 power of body weight; and for cattle with the 0.87 power of body weight[15].

It appears from Chs. 13 and 14 and from the above discussion that while we have some reliable data and agreement on the relation of basal metabolism to body weight, we have no correspondingly reliable data and agreement on the relation of maintenance energy to body weight. The reason for this deficiency in reliable maintenance data for animals of different size is, of course, the relatively great expense involved in maintaining such farm animals as cattle in statistically significant numbers in non-productive condition for statistically significant periods of time. There is particular need for maintenance data for mature animals of the same species, but differing widely in body weight. Dogs might furnish the desired range in body size, although it may be objected that dogs differing widely in body size may differ widely in their endocrines (Ch. 7) and consequently in their metabolism and maintenance needs for reasons other than body size as such.

It is obviously important to have precise data on maintenance in relation to body size for the scientific planning of national and institutional food needs for man, for formulating maintenance feeding standards for farm animals of various live weights, and for furnishing a basis for judging whether large and small farm animals differ in efficiency as converters of feed energy into the energy of desired products.

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[9] Haecker, T. L., Minn. Agr. Exp. Sta. Bull., 140, 1914; also Bull. 79, 1903, and 130, 1913.

[10] Morrison, F. B., "Feeds and feeding," Morrison Publishing Co., Ithaca, N. Y

[11] Savage, E. S., New York (Cornell) Agr. Exp. Sta. Bull. 323, 1912.

[12] Gaines, W. L., *J. Dairy Sci.*, **20,** 583 (1938).

[13] Eckles, C. H., Mo. Agr. Exp. Sta. Res. Bull. 7, 1913.

[14] Kriss, M., *J. Nut.*, **4,** 141 (1931); Cary, C. A., "Food and life", Yearbook of Agriculture, p. 655, 1939.

[15] Morrison, F. G., "Feeds and Feeding", pp. 77, 78, 81, and 1006, 1936. The 0.87 value of the exponent of W for cattle is the average of 1.0 of the old Henry-Morrison Standard and 0.74 which is the average of Kleiber's (0.75) and the writer's (0.73) value of the exponent $(1 + 0.74)/2 = 0.87$. We shall show later (Ch. 24) that in mature horses of different size, Percheron and Shetland, the resting metabolism varies more nearly with $W^{1.0}$ than with $W^{0.7}$.

The introductory discussion (also Chs. 3, 21, and 23) and Crasemann's table previously cited indicate that the energetic efficiency of a productive process, such as milk production, is independent of body weight, *provided* that both the maintenance energy cost and the energy equivalent of the product vary in the same manner with increasing body weight, for example with $W^{0.7}$; but there is no agreement on this. The writer and, as previously noted, Kleiber and Crassemann believe that, when other conditions are equal, maintenance and production run parallel, and that both vary with $W^{0.7}$ (the writer) or $W^{3/4}$ (Kleiber).

Gaines[16], on the other hand, believes that both milk production and maintenance cost are directly (linearly) proportional to simple body weight at the beginning of the lactation period. This, however, contradicts the fact that while superior 120-lb goats produce 10–15 lbs milk a day, 1200-lb superior cows produce not 100–150 lbs but only 50–60 lbs a day (Chs. 3, 21, and 22). Likewise, while the maintenance need of a 120-lb goat is of the order of 2 lbs *TDN* a day, the maintenance need of a 1200-lb cow is not 20 lbs but of the order of 10 lbs *TDN* a day.

So much for the energy cost of maintenance, which the writer believes varies approximately with $W^{0.7}$ rather than with simple body weight, $W^{1.0}$. The same is undoubtedly true of protein, since the ratio of endogenous or minimal nitrogen excretion to basal or minimal energy metabolism is approximately constant in animals ranging in weight from mice to cattle (Ch. 13), about 2 mg N/Cal.

As regards the maintenance needs for vitamins and trace elements, those that are involved in the general oxidation-reduction processes (Ch. 6) of intermediary metabolism, such as thiamine or riboflavin, undoubtedly vary directly with the energy metabolism, that is with the food-energy consumption, and if the energy metabolism varies with $W^{0.7}$, so must vitamin metabolism[17].

To illustrate by thiamine (vitamin B_1), the minimum vitamin required is estimated to be, on the basis of various types of data in the literature, in micrograms thiamine per 100 grams dry food, 80–100 for rats[18], 60 for chicks and turkeys[19], 75 for dogs[20], 50 to 90 for swine[21], 90 to 110 for man[22]. Exercise[23] and temperature[24], which increase energy metabolism, increase the thiamine need proportionately. Hyperthyroidism, which increases energy metabolism, also increases thiamine need[25]. In general, the minimal thiamine requirement (for man) is 0.3 to 0.5 mg per 1000 Cal metabolism, and the optimal is 0.5 to 1.0 mg per 1000 Cal metabolism[26]. The thiamine is thus proportional to the food-energy intake rather than body weight.

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[16] Gaines, W. L., *J. Dairy Sci.*, **20**, 583 (1939).

[17] Cowgill, G. R., "The vitamin B requirement of man", Yale Press, 1934. This was for "vitamin B" as a whole, requirement which author claimed to vary with $W^{0.66}$ in *mature* animals of *different species*, but (according to the reviewer's computation from Cowgill's data) with $W^{2.2}$ for *growing* mice, $W^{1.75}$ for *growing* rats, $W^{1.74}$ for *growing* pigeons, $W^{1.69}$ for *growing* dogs.

[18] Arnold, A., and Elvehjem, C. A., *J. Nut.*, **15**, 429 (1938).

It is similarly reasonable to assume that riboflavin (the prosthetic group of the yellow enzyme) is required in proportion to the oxidation rate, to energy metabolism, and therefore to the food or feed intake rather than to body weight. This assumption is justified by the following estimates of minimal requirement of riboflavin in micrograms per gram dry food: rats[27] and poultry[28], 100 to 200; dogs[29], 200 to 400; swine[30], 50 to 150.

If the above and other data are represented in terms of micrograms per unit body weight, the uniformity disappears and, like metabolism per unit weight, the larger the animal the smaller this ratio of vitamin B_2 to body weight.

Animal	Riboflavin need (mcg/100 gm body wt)
Rat	100–200
Chick	150–300
Hen	50–150
Dog	10–20
Swine	2–6
Man[31]	4–6

The data are too few to justify discussing the relation of the other members of the vitamin B complex to body weight. One would guess, however, that the pyridoxine and nicotinic acid requirements would vary with the energy metabolism rather than with simple body weight. The situation is complicated by the fact that many B vitamins are synthesized in the digestive tract.

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[19] Arnold and Elvehjem, *Id.*, **15**, 403 (1938).

[20] Arnold and Elvehjem, *Am. J. Physiol.*, **126**, 289 (1939).

[21] Hughes, E. H., *J. Nut.*, **20**, 239 (1940). Van Etten, C., Ellis, N. R., and Madsen, L. L., *J. Nut.*, **20**, 607 (1940).

[22] Williams, R. D., Mason, H. L., Smith, B. F., and Wilder, R. M., *Arch. Int. Med.*, **69**, 721 (1942); Knott, E. M., *Proc. Soc. Exp. Biol. and Med.*, **45**, 765 (1940).

[23] Guerrant, N. B., and Dutcher, R. A., *J. Nut.*, **20**, 589 (1940).

[24] Mills, C. A., *Am. J. Physiol.*, **133**, 525 (1941).

[25] Drill, V. A., and Overman, R., *Am. J. Physiol.*, **135**, 474 (1942). Sure, B., *J. Nut.*, **7**, 547 (1934), and **13**, 513 (1937).

[26] Williams, R. D., Mason, H. L., and Wilder, R. M., *Arch. Int. Med.*, **69**, 721 (1942).

[27] Supplee, G. C., Bender, R. C., and Kahlenberg, O. J., *J. Nut.*, **20**, 109 (1940). Mannering, G. J., Lipton, M. A., and Elvehjem, C. A., *Proc. Soc. Exp. Biol. and Med.*, **46**, 100 (1941).

[28] Morris, L. C., *et al.*, N. Y. (Cornell) Agr. Exp. Sta. Bull. 660, 1936. Jukes, T. H., *Poultry Sci.*, **17**, 227 (1938). Heuser, G. F., *et al.*, *Id.*, **17**, 105 (1938). Hunt, C. H., *et al.*, *Id.*, **17**, 87 (1938).

[29] Axelrod, A. E., Lipton, M. A., and Elvehjem, *Am. J. Physiol.*, **128**, 703 (1939).

[30] Hughes, E. H., *J. Nut.*, **20**, 233 (1940).

[31] Sebrell, W. H., *et al.*, *U. S. Public Health Service, Public Health Reports*, **56**, 510 (1941).

Curiously enough, ascorbic acid (vitamin C) metabolism is said to vary with body weight[32] rather than with energy metabolism. Still, guinea pigs are said to require 6 to 7 mg ascorbic acid per kg body weight, or perhaps 5 mg per kilo[33], whereas adult man and older children are said to require only 0.7 to 1.6 mg per kg body weight per day[34]; increasing metabolism by thyroxine increases the ascorbic acid requirements accordingly[35].

As regards the minimal requirement of the fat-soluble vitamins, it is definitely established[36] that the requirement for vitamin A varies directly with simple weight, $W^{1.0}$, and not with metabolism, $W^{0.7}$. The minimal vitamin A (not carotene) is 2 to 4 micrograms per pound live weight per day in such diverse species as rats, dogs, swine, sheep, cattle, and horses[36]. The situation is more complicated when feeding carotene (rather than vitamin A) because of species and perhaps individual differences in ability to utilize carotene. Thus rats, sheep, cattle, horses, and perhaps swine utilize carotene quite well, requiring about 10 micrograms carotene per pound body weight per day[36]; chickens [37] require about 50 micrograms carotene per pound per day, although the vitamin A requirements are virtually the same for both groups.

We conclude this chapter with a "maintenance standard" for energy and protein need of animals ranging in size from 0.1 to 1000 kg and with related items.

This "maintenance standard", presented in Table 15.1 and Figs. 15.1 and 15.2, is based on *digestible* energy (TDN = total digestible nutrients, assuming that 1 lb TDN is equivalent to 1814 digestible Calories; one gram TDN is equivalent to 4 Cal; 1 gram protein and carbohydrate have heat equivalents of 4 Cal and 1 gram fat, 9 Cal) and *digestible* crude protein (DCP = "digestible" N × 6.25). By employing the *digestible* nutrient category, complications associated with fecal losses are apparently not actually avoided.

This "standard" is based on the assumption that both the energy and nitrogen metabolism vary with $W^{0.73}$ rather than with $W^{1.0}$; and that the maintenance need for digestible energy, TDN, is double the basal-energy metabolism and that the digestible crude protein, DCP, is four times the protein equivalent of the endogenous urinary excretion.

In Figs. 15.1 and 15.2 the heavy curves designated by (A) represent basal metabolism, or endogenous urinary nitrogen. The lighter curves designated by (2A), (3A), and (4A) represent 2, 3, and 4 times the basal levels. The broken curves represent Henry and Morrison's feeding standards (1923) for maintenance, which increases *directly* with body weight (curves A, 2A, etc. increase with the 0.73 power of body weight).

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[32] Dann, M., and Cowgill, G. R., *J. Nut.*, **9,** 507 (1934).

[33] Herman, M. T., and Miller, P., *Kans. Acad. Sci.*, **42,** 445, 1939. Zilva, S. S., *Biochem. J.*, **30,** 1419 (1936).

[34] Smith, S. L., U.S.D.A. Yearbook, p. 235, 1939.

[35] Demole, V., and Ippen, F., *Z. Physiol. Chem.*, **235,** 226 (1935). Oehme, C., *Klin. Wchnschr.*, **15,** 512 (1936).

[36] Guilbert, H. R., Howell, C. E., and Hart, G. H., *J. Nut.*, **19,** 91 (1940). Hart, G. H., *Nut. Abs. and Rev.*, **10,** 261 (1940).

[37] Frohring, W. O., and Wyeno, J., *J. Nut.*, **8,** 463 (1934). Sherwood, R. M., and Fraps, G. S., Texas Agr. Exp. Sta. Bull. 528, 1936, and 583, 1940.

These "standards" are in agreement with the usual 3000 Cal and 70 to 80 grams protein maintenance allowance for a 70-kg man, and with Henry and Morrison's 1923 maintenance standard for about 500-pound farm animals.

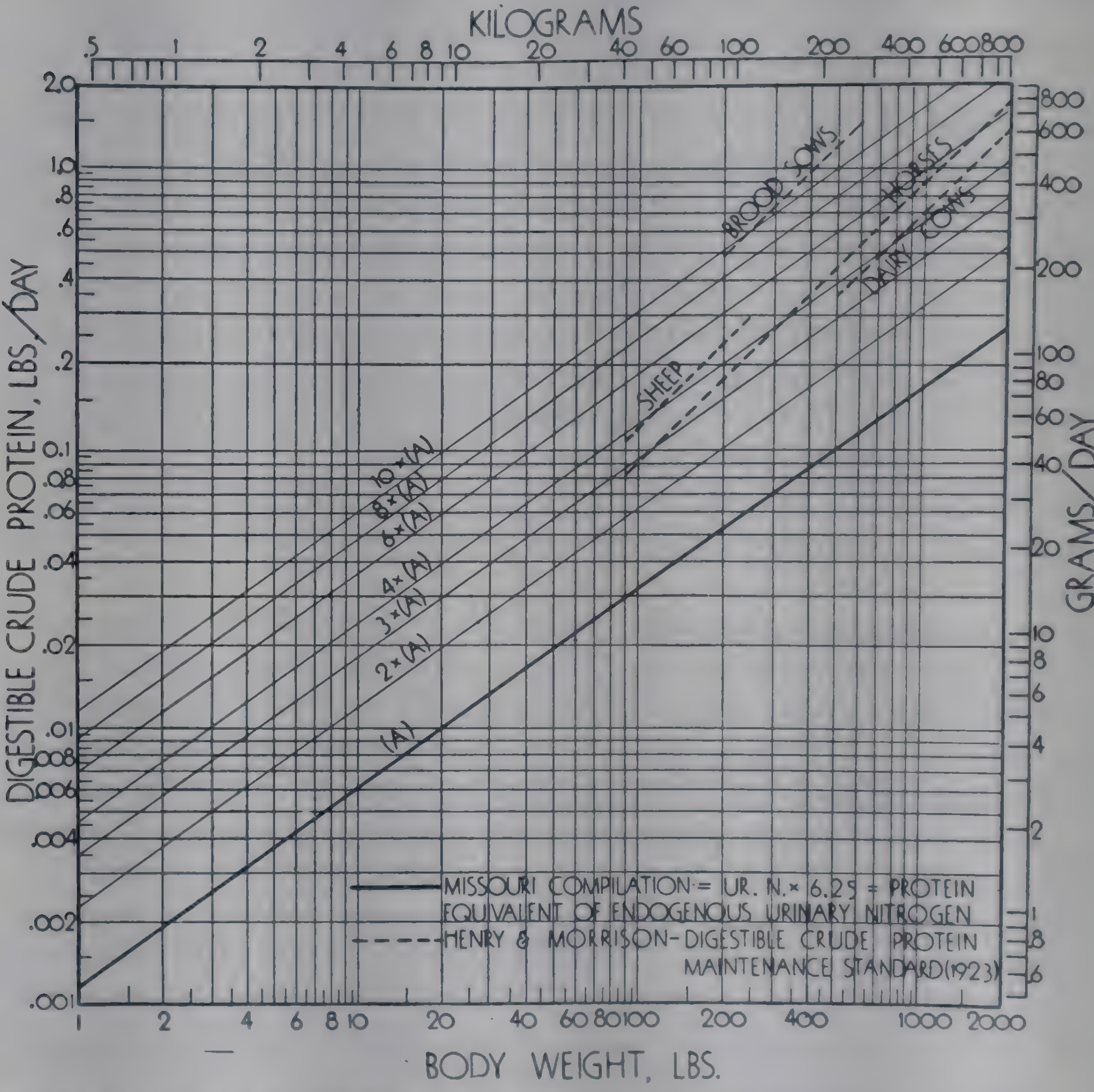


Fig. 15.1. Line (A) designates the DCP (digestible crude protein) equivalent of urinary endogenous nitrogen excretion (1 unit DCP is equivalent to 6.25 units urinary endogenous nitrogen). Lines 2x(A), 3x(A), etc. designate respectively 2, 3 . . . times the urinary endogenous level curve. Line 4x(A), representing 4 times the endogenous DCP equivalent, is the proposed DCP standard for maintenance. The broken curve represents the 1923 Henry and Morrison maintenance standard.

Our "standard" is probably equally applicable to all species of warm-blooded animals, from mice to elephants: maintenance per unit weight declines with increasing weight not only as regards energy (or *TDN*) but also as regards nitrogen (or *DCP*). As previously noted, the need for general-oxidation reduction biocatalysts (as thiamine and riboflavin, etc.) perhaps vary in similar, $W^{0.7}$, fashion.

While the "standard" in Table 15.1 and Figs. 15.1 and 15.2 is based on the assumption that the maintenance need for *TDN* calories is twice the basal-metabolism calories given in Table 13.7, we have computed (Ch. 21) the maintenance *TDN* of lactating cows by a different method—by algebraic (least squares) partitioning of the *TDN* consumed between its uses for: (1) milk production, (2) maintenance, and (3) weight gain or loss. Such algebraic partitioning of the *TDN* consumed by 243 good lactating cows gave 8.2 lbs *TDN* for maintaining a 1000-lb lactating cow. It is interesting to compare this maintenance value with those arrived at by other investigators employing other methods.

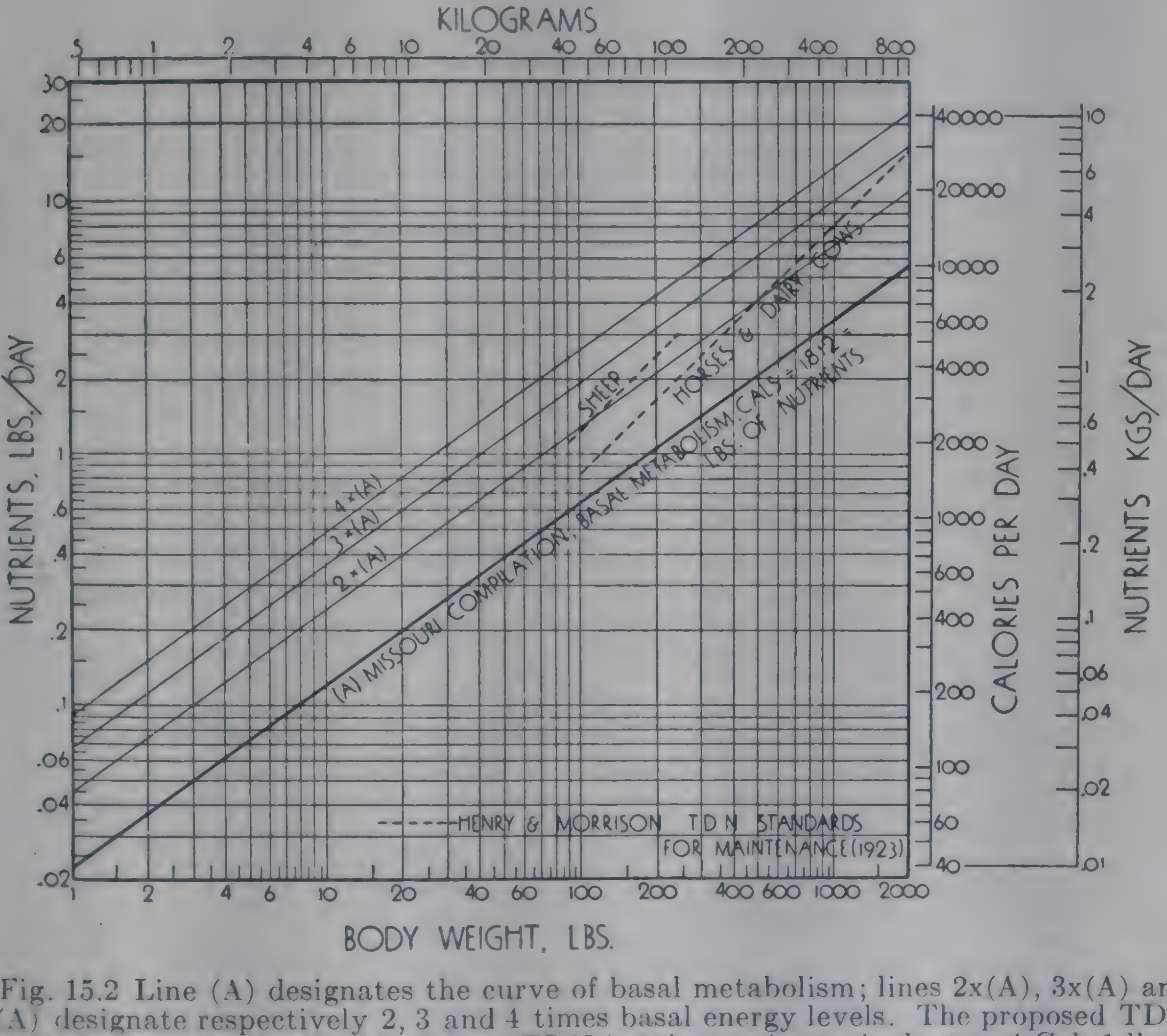


Fig. 15.2 Line (A) designates the curve of basal metabolism; lines 2x(A), 3x(A) and 4x(A) designate respectively 2, 3 and 4 times basal energy levels. The proposed TDN standard represents curve 2A. (1 gm TDN is taken to be equivalent to 4 Cal, 1 lb to 1812 Cal). The broken curve represents the 1923 Henry and Morrison standard for TDN.

Fig. 15.3 shows Gaines[16] graphic comparison of the various maintenance feeding standards with our suggested maintenance standard for lactating cows. The results are expressed in terms of pound *TDN* per 1000-lb live weight of cow. Frederiksen's curve is based on the assumption that *TDN* need for maintenance is proportional to $W^{2/3}$; the author's, that it is proportional to $W^{0.73}$; Morrison's (1936 ed.) that it is proportional to $W^{0.87}$. The

Table 15.1 Feeding Standards for Maintenance.*

Body wt. (lbs)	Pound System						Body wt. (kg)	Gram System					
	TDN (lbs)		*DCP* (lbs)		*TDN* (Cals)			*TDN* (gms)		*DCP* (gms)		*TDN* (Cals)	
	Per animal	Per 1000 lbs	Per animal	Per 1000 lbs	Per animal	Per lb		Kgs. per animal	Gms. per kg.	Per animal	Per kg.	Per animal	Per kg.
2000	11.20	5.60	1.16	.580	20300	10.2	1000	5.45	5.45	564	.564	21800	21.8
1900	10.79	5.68	1.12	.589	19500	10.3	900	5.05	5.61	524	.582	20200	22.4
1800	10.37	5.76	1.07	.595	18800	10.4	850	4.85	5.71	504	.593	19400	22.8
1700	9.95	5.85	1.03	.606	18000	10.6	800	4.63	5.79	480	.600	18500	23
1600	9.52	5.95	.988	.617	17300	10.8	750	4.43	5.91	460	.613	17700	23.6
1500	9.08	6.05	.941	.627	16500	11.0	700	4.23	6.04	436	.623	16900	24.1
1400	8.63	6.16	.894	.639	15600	11.1	650	3.97	6.11	412	.634	15900	24.5
1300	8.18	6.29	.848	.652	14800	11.4	600	3.77	6.28	390	.650	15100	25.2
1200	7.71	6.43	.801	.667	14000	11.7	550	3.53	6.42	366	.665	14100	25.6
1100	7.24	6.58	.750	.682	13100	11.9	500	3.27	6.54	341	.682	13100	26.2
1000	6.75	6.75	.699	.699	12200	12.2	450	3.05	6.78	316	.702	12200	27.1
900	6.25	6.94	.648	.720	11300	12.5	400	2.80	7.00	290	.725	11200	28.0
800	5.74	7.17	.594	.743	10400	13.0	350	2.53	7.23	263	.751	10100	28.9
700	5.21	7.44	.539	.770	9440	13.5	300	2.26	7.53	235	.783	9050	30.2
600	4.65	7.75	.480	.800	8430	14.1	250	1.99	7.96	206	.824	7950	31.8
500	4.07	8.14	.422	.844	7375	14.7	200	1.69	8.45	175	.875	6750	33.7
400	3.46	8.65	.359	.897	6270	15.7	150	1.36	9.07	142	.947	5450	36.3
350	3.14	8.97	.325	.929	5690	16.3	125	1.20	9.60	128	1.02	4790	38.3
300	2.80	9.33	.291	.970	5070	16.9	100	1.02	10.2	105	1.05	4070	40.7
250	2.45	9.80	.254	1.02	4440	17.8	90	.943	10.5	97.6	1.08	3770	41.9
200	2.09	10.45	.216	1.08	3790	18.9	80	.863	10.8	89.6	1.12	3450	43.1
150	1.69	11.27	.175	1.17	3060	20.4	70	.783	11.2	81.2	1.16	3130	44.7
125	1.48	11.84	.153	1.22	2680	21.4	60	.700	11.7	72.4	1.21	2800	46.7
100	1.26	12.60	.130	1.30	2283	22.8	50	.613	12.3	63.6	1.27	2450	49.0
75	1.02	13.60	.106	1.41	1850	24.1	40	.523	13.1	54.0	1.35	2090	52.3
50	.758	15.16	.0785	1.57	1370	27.4	30	.423	14.1	43.6	1.45	1690	56.3
25	.457	18.28	.0473	1.89	828	33.1	20	.313	15.7	32.5	1.63	1250	62.5
10	.234	23.40	.0243	2.43	424	42.4	10	.189	18.9	19.6	1.96	755	75.5
9	.217	24.11	.0225	2.50	393	43.7	9	.175	19.4	18.2	2.02	700	77.8
8	.199	24.87	.0206	2.57	361	45.1	8	.161	20.1	16.7	2.09	645	80.6
7	.181	25.86	.0191	2.73	328	46.9	7	.146	20.9	15.1	2.16	585	83.6
6	.161	26.83	.0167	2.78	292	48.7	6	.130	21.7	13.5	2.25	520	86.7
5	.141	28.20	.0146	2.92	255	51.0	5	.114	22.8	11.8	2.36	457	91.4
4	.120	30.00	.0124	3.10	217	54.3	4	.0970	24.3	10.0	2.50	388	97.0
3	.0972	32.40	.0101	3.37	176	58.7	3	.0787	26.2	8.16	2.72	315	105
2	.0723	36.15	.00750	3.75	131	65.5	2	.0585	29.3	6.04	3.02	234	117
1	.0436	43.60	.00453	4.53	79.0	79.0	1	.0353	35.3	3.65	3.65	141	141
.9	.0404	44.89	.00418	4.64	73.2	81.3	.9	.0327	36.3	3.38	3.75	131	145
.8	.0371	46.38	.00384	4.80	67.2	84.0	.8	.0300	37.5	3.10	3.87	120	150
.7	.0336	48.00	.00348	4.97	60.9	87.0	.7	.0273	39.0	2.82	4.03	109	156
.6	.0300	50.00	.00311	5.18	54.4	90.7	.6	.0243	40.5	2.52	4.20	97.0	162
.5	.0263	52.60	.00273	5.46	47.6	95.2	.5	.0213	42.6	2.20	4.40	85.0	170
.4	.0223	55.75	.00232	5.80	40.4	100.1	.4	.0181	45.3	1.87	4.67	72.5	181
.3	.0181	60.33	.00187	6.23	32.8	109.3	.3	.0146	48.7	1.52	5.07	58.5	195
.2	.0135	67.50	.00139	6.95	24.5	122.5	.2	.0109	54.5	1.13	5.65	43.5	217
.1	.0081	81.00	.00084	8.40	14.7	147.0	.1	.0065	65.0	.068	6.80	26.0	260

* Computed from equation $Y = AM^{0.73}$ in which Y represents *TDN* (total digestible nutrients per day = digestible crude protein + digestible carbohydrates + digestible fat × 2.25), or *DCP* (digestible crude protein per day = N × 6.25) for body weight M, and from the assumptions that *TDN* energy (4 Cal. per gram or 1812 Cal. per pound) is twice basal-metabolism energy, and *DCP* is four times the *DCP* equivalent of endogenous urinary nitrogen. (The nutritive ratios are thus always 1:8.7 or what is the same, 10.34%, of the total calories, or of the *TDN*, is in the form of protein.)

other curves are based on the assumption that maintenance varies with $W^{1.0}$ *i.e.*, with simple body weight. Fig. 15.4 compares our proposed standard

Table 15.2 Estimated maintenance cost of chickens

Live weight		Maintenance feed cost/day		Live weight		Maintenance feed cost/day		Live weight		Maintenance feed cost/day		Live weight		Maintenance feed cost/day	
(lb)	(gm)	(gm)	(lb)	(lb)	(gm)	(gm)	(lb)	(lb)	(gm)	(gm)	(lb)	(lb)	(gm)	(gm)	(lb)
¼	113	9.5	.021	2¾	1247	54.6	.120	5¼	2381	87.5	.193	7¾	3515	116	.256
½	227	15.7	.035	3	1361	58.2	.128	5½	2495	90.6	.200	8	3629	119	.262
¾	340	21.1	.047	3¼	1474	61.7	.136	5¾	2608	93.4	.206	8¼	3742	122	.269
1	454	26.1	.058	3½	1588	65.1	.144	6	2722	96.5	.213	8½	3856	123	.272
1¼	567	30.7	.068	3¾	1701	68.5	.151	6¼	2835	99.4	.220	8¾	3969	127	.280
1½	680	25.1	.077	4	1814	71.8	.158	6½	2948	102	.226	9	4082	130	.286
1¾	794	39.3	.087	4¼	1928	75.0	.165	6¾	3062	105	.232	9¼	4196	132	.292
2	907	42.3	.095	4½	2041	78.2	.172	7	3175	108	.238	9½	4309	135	.298
2¼	1021	47.2	.104	4¾	2155	81.3	.179	7¼	3288	111	.244	9¾	4473	138	.303
2½	1134	50.9	.112	5	2268	84.5	.186	7½	3402	114	.250	10	4536	140	.309

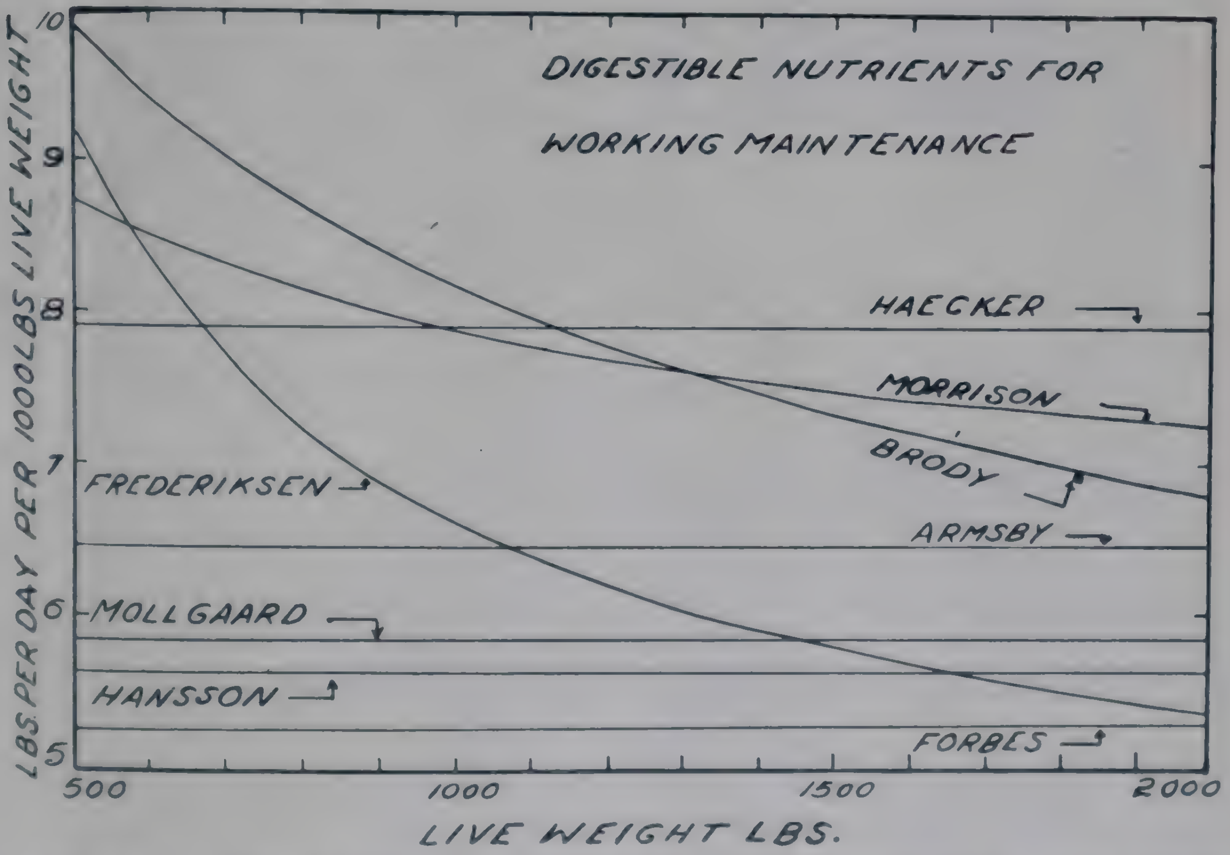
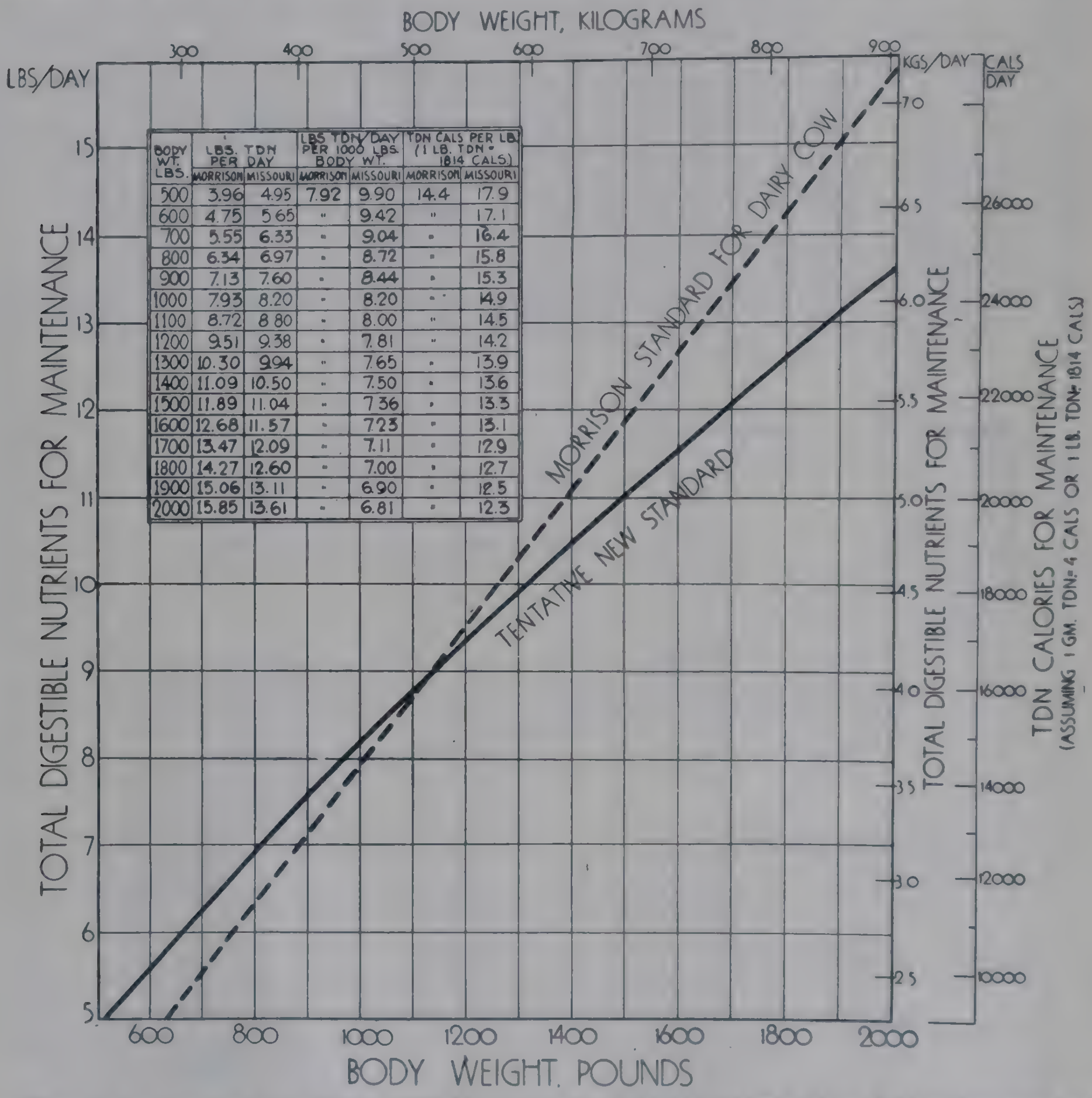


Fig. 15.3. "Digestible nutrients required for working maintenance of dairy cows of various live weight, according to 8 different feeding standards". Curves and legend from W. L. Gaines, *J. Dairy Sci.*, **20**, 591 (1937).

for cows of different weight with Morrison's 1923 standard, which is, of course, the standard of Haecker and was also adopted by Savage, Gaines, and others.

As previously noted, Haecker, on the basis of one of the best and best known investigations in this field, proposed a maintenance feeding standard of 7.925 lbs—8.0 lbs in round numbers—*TDN per* 1000 lbs live weight of dairy cow, regardless of the weight of the cow and this value was adopted by Savage, Morrison (1923 ed.) and Gaines. This value, 8.0, arrived at by observing maintenance needs of *non-lactating* cows, is somewhat below our value, 8.2, arrived at by the algebraic-partition method for 243 *lactating* cows described in Chapter 21, and is considerably higher than our estimated value of 6.75 in Table 15.1, based on the assumption that the maintenance *TDN* Calories is twice the basal-metabolism of *non-lactating* mature animals of different species. It is, of course, reasonable that lactating animals should have a higher maintenance cost than non-lactating. Our 6.75 value (Table 15.1) for a 1000-lb non-lactating animal is almost identical with Kellner's standard of 6.7 lbs *TDN* for a 1000-lb cow. (The other maintenance stand-



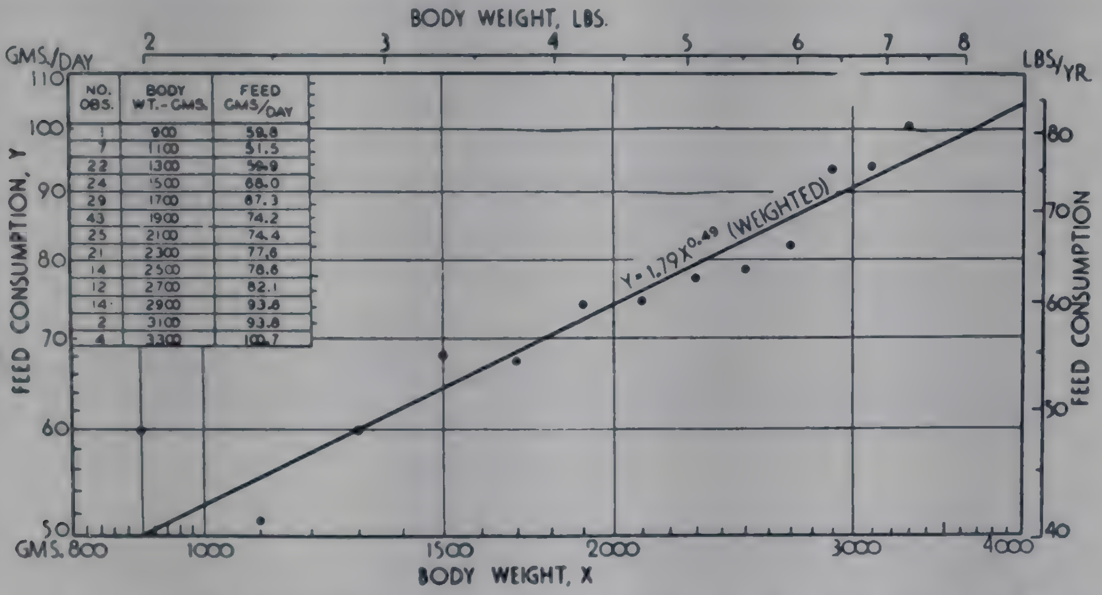
BODY WT. LBS.	LBS. TDN PER DAY		LBS TDN/DAY PER 1000 LBS. BODY WT.		TDN CALS PER LB. (1 LB. TDN = 1814 CALS.)	
	MORRISON	MISSOURI	MORRISON	MISSOURI	MORRISON	MISSOURI
500	3.96	4.95	7.92	9.90	14.4	17.9
600	4.75	5.65	"	9.42	"	17.1
700	5.55	6.33	"	9.04	"	16.4
800	6.34	6.97	"	8.72	"	15.8
900	7.13	7.60	"	8.44	"	15.3
1000	7.93	8.20	"	8.20	"	14.9
1100	8.72	8.80	"	8.00	"	14.5
1200	9.51	9.38	"	7.81	"	14.2
1300	10.30	9.94	"	7.65	"	13.9
1400	11.09	10.50	"	7.50	"	13.6
1500	11.89	11.04	"	7.36	"	13.3
1600	12.68	11.57	"	7.23	"	13.1
1700	13.47	12.09	"	7.11	"	12.9
1800	14.27	12.60	"	7.00	"	12.7
1900	15.06	13.11	"	6.90	"	12.5
2000	15.85	13.61	"	6.81	"	12.3

Fig. 15.4. Comparison of the 1923 Morrison feeding standard (also of Haecker, and of Savage) with our proposed (Missouri) standard.

ards, for a 1000-lb cow are, as previously noted, 8.0 (Haecker, Savage, Gaines, Morrison), 7.5 (Eckles), 6.7 (Kellner), 6.5 (Armsby), 6.0 (Forbes and Kriss), 5.9 (Möllgaard), 5.7 (Hansson).

It may be observed that our algebraic-partition method (Ch. 21) also gave a *TDN* need per pound of *FCM* (milk containing 4 per cent fat) produced which agrees well with other standards. Our partition method allows 0.305 lb *TDN* per pound *FCM*; Gaines' standard allows 0.3 lb, which was abbreviated from Haecker's 0.327; Armsby, 0.285; Forbes and Kriss, 0.30; Morrison, 0.307 to 0.324; Möllgaard, 0.302; Hansson, 0.302.

It is instructive to note in conclusion that records were kept of feed consumption of mature chickens of different live weight during 28-day intervals when they were not laying eggs.[38] The results, shown in Fig. 15.5, indicate, to our surprise, that the feed consumption increased not with $W^{1.0}$ as poultrymen generally believe, nor with $W^{0.73}$ as we expected, nor with $W^{2/3}$ as others might expect, but with $W^{0.5}$. These unexpected results will have to be confirmed before acceptance.



NO. OBS.	BODY WT.-GMS.	FEED GMS/DAY
1	900	59.8
7	1100	51.5
22	1300	59.9
24	1500	68.0
29	1700	67.3
43	1900	74.2
25	2100	74.4
21	2300	77.6
14	2500	78.6
12	2700	82.1
14	2900	93.6
2	3100	93.8
4	3300	100.7

Fig. 15.5. The feed consumption of domestic fowls during non-laying 28-day periods increased with, roughly, the 0.5 power of body weight, *i.e.*, increasing body weight by 100 per cent increased feed consumption by about 50 per cent.

The partition-equation method employed for evaluation of feed distribution between maintenance and egg production (Ch. 23) based on the assumption that feed cost of maintenance varies with the 0.73 power of body weight, yields, for maintenance, the equation

$$Y = 0.30W^{0.73}$$

in which Y is grams of the chicken feed expended for maintaining body weight in grams, W. Table 15.2 gives the computed values for maintenance of chickens of different live weight.

Titus[39] reported that "the gross maintenance requirement of White Leghorn hens, 16 months old and weighing, on an average, 1632 grams, was estimated as being 64 grams (of the special feed mixture) per bird per day during July". The corresponding maintenance feed requirement for a 1632-gram bird, as indicated in our Table 15.2 is 66.3

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[38] Brody, S., Funk, E. M., and Kempster, H. L., Mo. Res. Bull. 278, 1938.

[39] Titus, H. W. *Poultry Science*, **8**, 80 (1928–29).

grams, and from the table in Fig. 15.5, 67.2 grams. The three values agree satisfactorily among themselves.

By way of somewhat indirect substantiation on the way total metabolism varies with body weight, data from the literature on egg weight and body weight are brought together in Fig. 15.6. The data ranged from 0.6 gram humming-bird eggs to 1700-gram (nearly 4-lb) ostrich eggs.

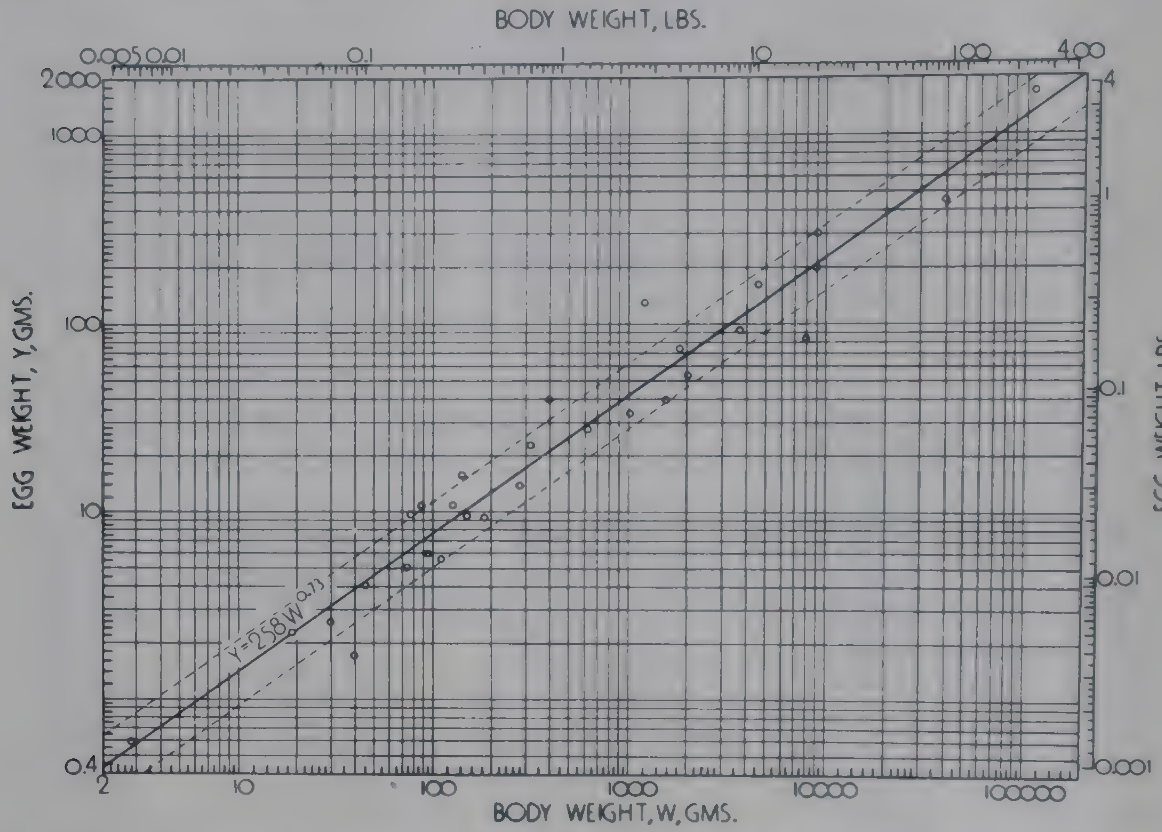

Fig. 15.6. The relation between egg and body weights of different bird species ranging in body weight from 113.4 kg (250-pound) ostrich to a 2.8-gm (0.10-oz) humming bird, and ranging in egg weight from 1.7 kg (3.75-lb) ostrich to 0.6-gm (0.02-oz) humming-bird egg. The X^s (Kiwi) are not included in the equation, fitted to the data by the method of least squares. With the exception of the data for the quail, turkey, goose, and duck, which are original (Mo. Res. Bul. 278), the data were plotted from Bergtold's compilation (see text). The numerical data (first value gm body weight, second, gm egg weight) are: Ostrich (113,380-1700); Emperor Penguin (40,817-454); Toulouse goose (9072-200.8); California vulture (9070-309); Turkey (8172-85); Chinese goose (4536-165.4); Pekin duck (3629-94.5); one domestic fowl included in general equation (2041-72); Runner duck (1814-75.6); Kiwi *not included in equation* (1814-41 and 1701-397); guinea hen (1587-40); Adelie penguin (1205-130); Ring-neck pheasant (1020-34); Golden pheasant (624-28); yellow-billed tropic bird (397-40); long-eared owl (320-23); domestic pigeon (283-14); quail (185-9.4); Magpie (151-9.6); Screech owl (142-16); mourning dove (128-11); Meadow lark (113-5.7); Western robin (95-6.0); Kildeer (88-11); Western nighthawk (78-9.9); Brewer's blackbird (74-5.1); Kingbird (45-4.1); Catbird (40-1.7); English sparrow (30-2.6); House finch (19-2.3); Broad-tailed humming bird (2.8-0.6).

Fig. 15.6, based on Bergtold's compilation,[10] and on data on the domestic fowl, quail, turkey, duck and goose furnished by E. M. Funk of this Station, shows that as between different species, egg weights increase with the 0.73 power of body weight, at practically the same rate as basal metabolism of mature animals of different species. This is an exceedingly interesting result. The wide scatter of the data should not be disturbing, considering the fact that in many cases the body weights were taken from one observer, and the eggs from another, and that a change in body weight, due to increase or decrease in body fat, does not appreciably affect the *egg* size. This increase in egg weight with $W^{0.73}$ rather than with $W^{1.0}$, indicates to the writer that the total metabolism parallels the basal metabolism, and what is true of egg production is likely to be true of other productive processes. A similar result was found (Ch. 22) for milk production in rats, goats, cattle, and man.

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[10] Bergtold, H., "A study of incubation period of birds. What determines their length?" The Kendrick-Bellamy Co., Denver, Colorado, 1917.

Summarizing this chapter, while we have reliable data on basal energy and endogenous nitrogen (Chs. 13 and 14), we do not have data of comparable reliability on the maintenance cost. It appears, however, that the maintenance needs for energy, protein, and dietary catalysts (*e.g.*, thiamine and riboflavin) which participate in the general oxidation processes vary in the same manner as the basal energy and endogenous nitrogen metabolism, namely with approximately $W^{0.7}$.

To be sure some types of metabolism vary directly with simple body weight. This is true of creatinine, which is a part of the endogenous-nitrogen metabolism varying with $W^{0.7}$, yet itself varies with $W^{1.0}$, in both mature animals of different species and in the same animals when growing. About 15 mg creatinine are excreted per kilo body weight[41] in rats of all weights, and also in cattle and man. Likewise, as regards vitamin A, which is needed in proportion to $W^{1.0}$ rather than to $W^{0.7}$. The mineral need may be in proportion to body weight. But in general, those processes involving oxidation vary with $W^{0.7}$ rather than with $W^{1.0}$. The energy expense of muscular exercise varies in proportion to $W^{1.0}$ rather than to $W^{0.7}$ but, in most animals, increase in size is associated with decrease in the frequency and rapidity of movements, so that perhaps the energy expenditure for spontaneous exercise associated with a maintenance life varies with $W^{0.7}$ rather than with $W^{1.0}$. This reasoning, that total metabolism varies with basal metabolism or with $W^{0.7}$, is in harmony with dimensional analysis (Chs. 10 and 17) and with such observations as that milk production (Ch. 22) and egg production (Fig. 15.6) varies with $W^{0.7}$ rather than with $W^{1.0}$, and that the ratio of maximal food-energy intake to basal metabolism is independent of the size of the animal. There are exceptions in detail, but this appears to be the general rule.

[41] Ashworth, U. S., and Brody, S., Mo. Agr. Exp. Sta. Res. Bulls. 189, 190, and 191, 1933.

Chapter 16

Time Relations of Growth of Individuals and Populations

> All motion of natural action is performed in time. *F. Bacon*
>
> Everything exists not only in a frame of space but also in a pattern of time. *G. E. Coghill*
>
> As early as the fifth century B.C., Greek physicians developed a very clever method for the study of growth which is employed by scientists down to our day. A hen was set upon a number of eggs; each day one of these eggs was opened and the changes that took place could be observed. *H. E. Sigerist*

16.1: Introduction and definitions. The use of isotopes in the study of metabolic processes has shown that, perhaps, all constituents of the living cell are involved in continuous chemical reactions, continuous breaking down and building up—catabolism and anabolism. It is only the pattern, the life whirlpool, that endures. Biologic synthesis, that is, the interaction of exogenous material (food) in the formation of new chemical-morphological units, thus occurs not only during the period conventionally designated as growth, but throughout the entire life cycle[1].

The occurrence of widespread synthesis throughout life may also be observed without refined metabolic studies. Thus blood cells and epidermis have long been known to undergo rapid destruction and renewal; there is a continuous need for growth catalysts (hormones, vitamins, etc.) and structural materials (amino acids, minerals) to compensate for the continuous losses, breaking down, or catabolism, of the body. These constructive processes are more dramatic during periods following starvation and injury, especially regeneration of limbs in lower forms of life.

The most spectacular type of directed biosynthesis is, of course, growth and development, especially during embryonic life. Everyone has been impressed by the miraculous transformation of the sticky white and yellow mass of hen's egg into a fully dressed, befeathered, respectable chick, all in 21 days. The original egg cell must have travelled at a dizzy pace to build up so complex a mechanism—probably exceeding in complexity the astronomical wonders with their galaxies and supergalaxies.

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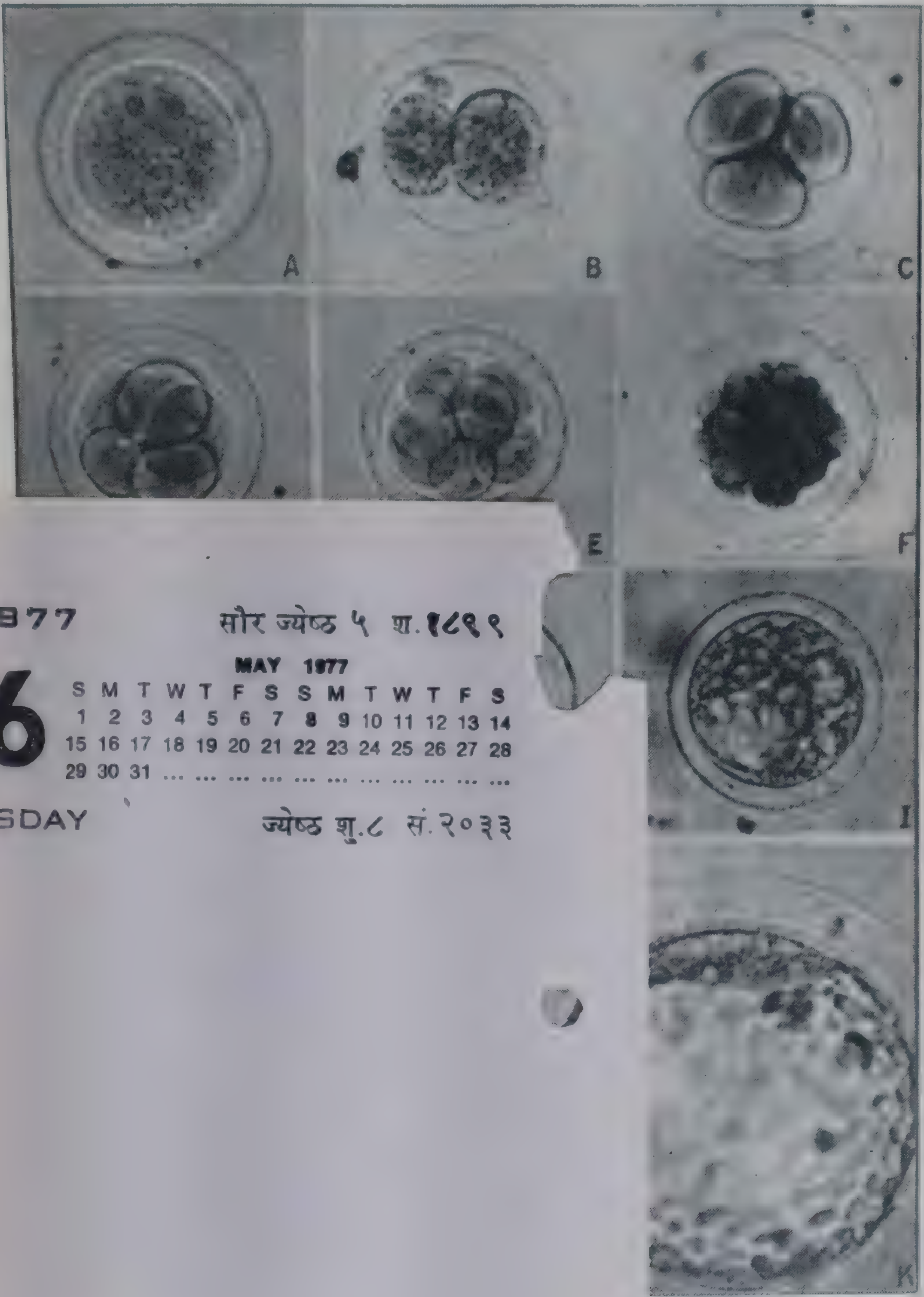
[1] Schoenheimer, Rudolph, *Physiol. Rev.*, **20,** 218 (1940); *Growth*, Second Supplement, p. 27 (1940); "Dynamic state of body constituents," Harvard University Press, 1942 (ed. by H. T. Clarke).

Growth as thus defined is inseparable from metabolism, and the several chapters in this book are merely different aspects of essentially the same problem, metabolism-growth. Thus Chapter 6 is concerned with enzymes in metabolism, in biologic synthesis; Chapter 7, with hormones; Chapters 13 to 15, with "maintenance" catabolism;



days after fertilization. A,
res, about 25 hours after; C,
8-cell stages 32 hours; F, 32-
cells, 71 hours; I, fluid collec-
egmentation cavity 90 hours;
rom P. W. Gregory [Plate I,
Carnegie Inst. Wash., 21, 107 (1930)], arranged by [illegible] Streeter [*Sci. Monthly*, **32**, 498 (1931)].

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S	M	T	W	T	F	S	S	M	T	W	T	F	S
1	2	3	4	5	6	7	8	9	10	11	12	13	14
15	16	17	18	19	20	21	22	23	24	25	26	27	28
29	30	31	...	...	...	...	...	...	...	...	...	...	...

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Chapter 20, with general nutritional aspects, and so on. This chapter is concerned with the definitions and time relations of average development and growth in weight of the body as a whole.

Development refers to the *directive* coordination of the diverse processes into an adult—into an "organized heterogeneity" (Needham). Some types of growth are not developmental: Teratomata are jumbles of hair, teeth, nerve, etc. Cancerous growth, like growth of tissue cultures *in vitro*[2], is without *directive* significance outside of self-multiplication.

Growth is biologic synthesis, production of new biochemical units. It is the aspect of development concerned with increase in living substance or protoplasm, and includes one or all of three processes: (1) cell multiplication, (2) cell enlargement, (3) incorporation of material taken from the environment. The cleavage of the egg into daughter cells is growth by cell multiplication, not by cell enlargement nor by incorporation of material from the outside. Blood corpuscles, monocytes, hair-follicle cells, and ectoderm cells always grow by cell multiplication. Nervous tissue and skeletal-muscle tissue grow by cell enlargement, not by cell division. The inclusion of non-protoplasmic substances, such as fat, blood plasma, cartilage, etc., is an increase by incorporation of

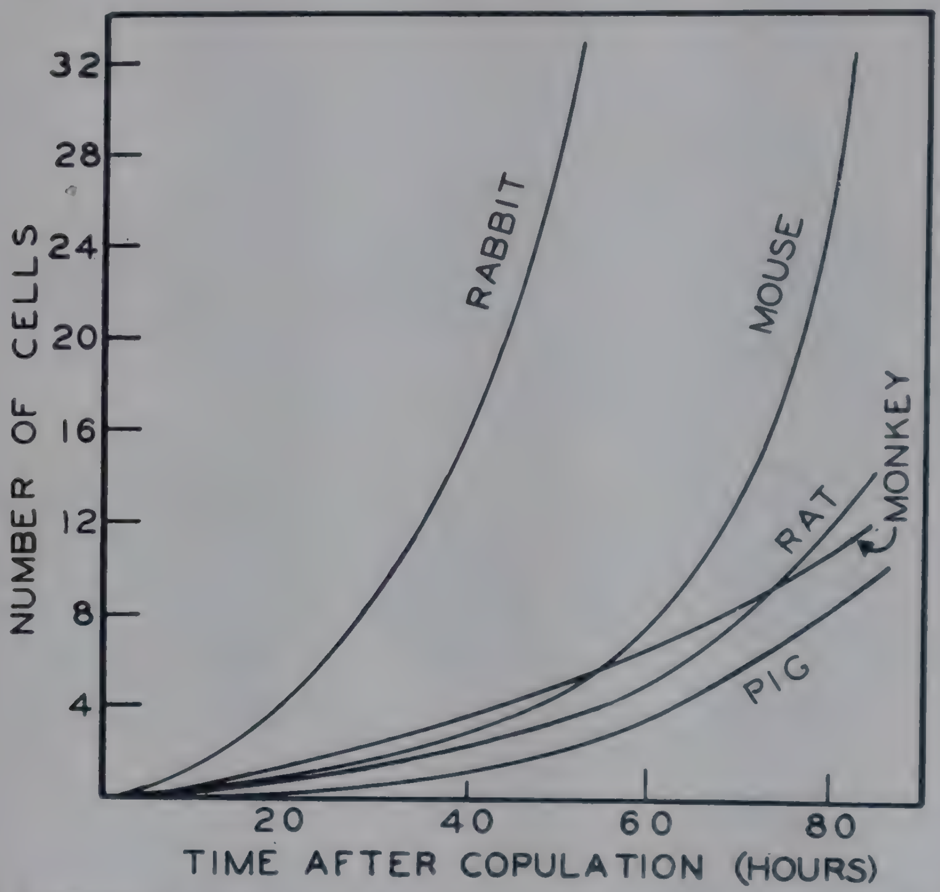

Fig. 16.2. Increase in cell number of tubal ova in several species, modified from Fig. 29, p. 89, "The Eggs of Mammals," Gregory Pincus, Macmillan Co., "Experimental Biology Series," New York, 1936, from data by Gregory (rabbit), Carnegie Inst. Wash., *Contrib. Embryol.*, **21**, 141 (1930), and Pincus, G., *Proc. Roy. Soc.*, **107**, 132 (1930); Lewis, W. H., and Wright, E. S., (mouse) Carnegie Inst. Wash., *Contrib. Embryol.*, **25**, 113 (1935); Lewis, W. H., and Hartman, C. G., (monkey) *Id.*, **24**, 187 (1933); Heuser, C. H., and Streeter, G. L., (pig) *Id.*, **20**, 1 (1929); Gilchrist, F., and Pincus, G., (rat) *Anat. Rec.*, **54**, 275 (1932).

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[2] *Cf.* Lewis, W. H., "Symposium on Development and Growth," First Supplement to *Growth* (1939).

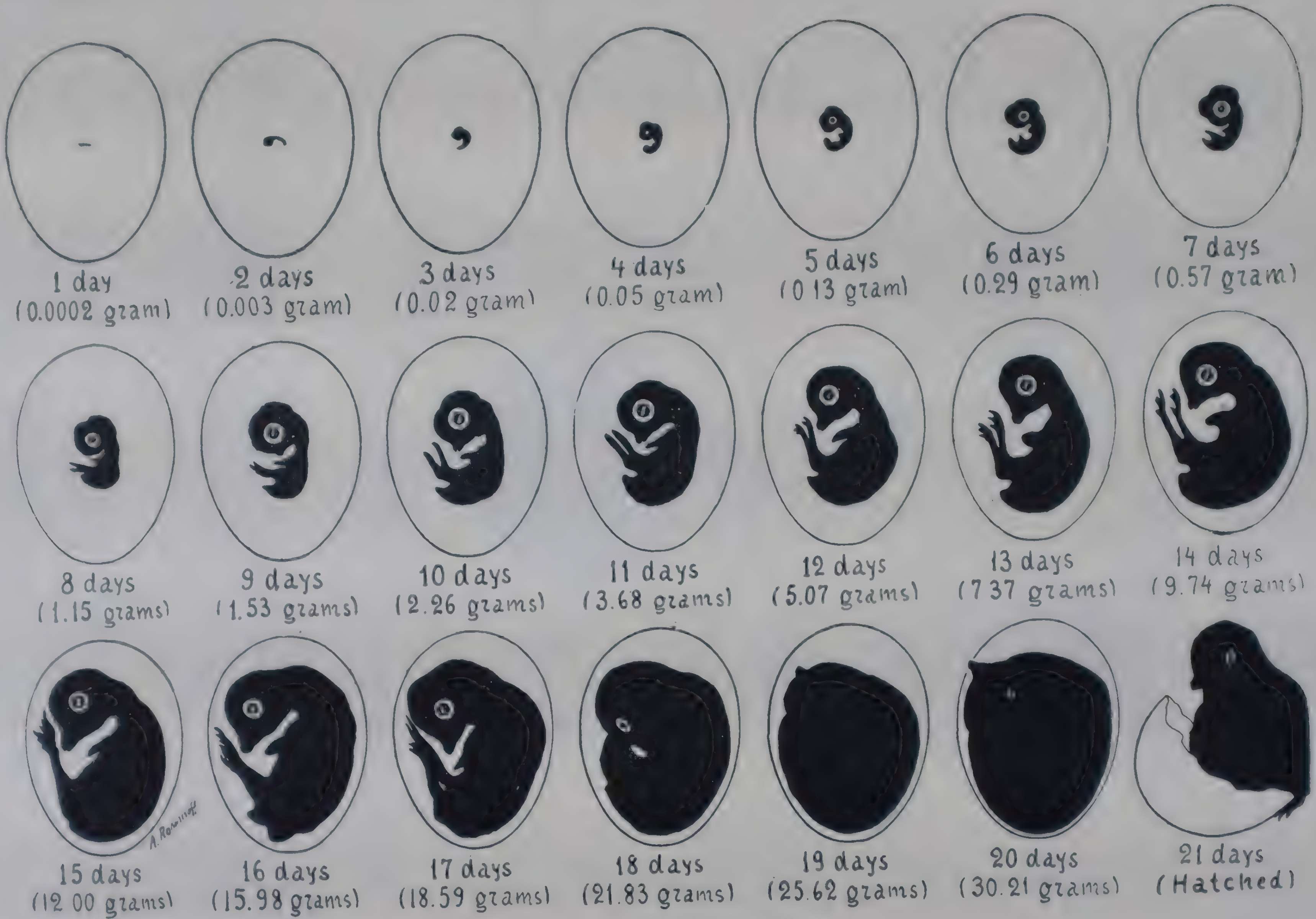
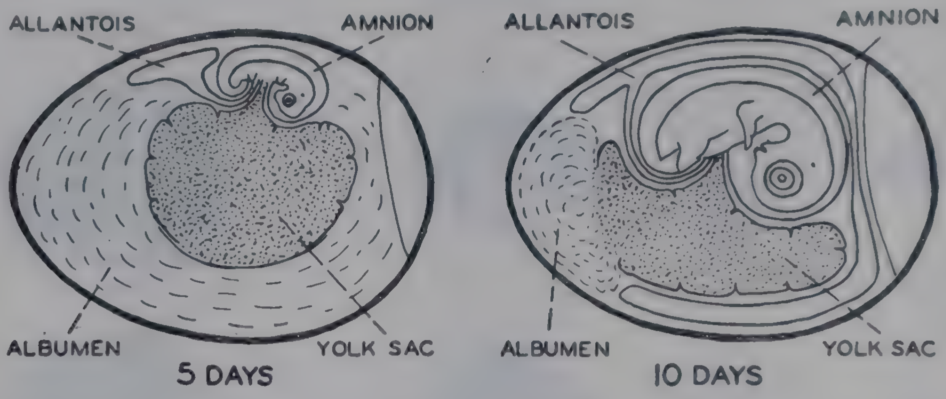


Fig. 16.3a—See legend for Fig. 16.3b

material from the environment, involving neither cell multiplication nor cell enlargement. Such increase is not regarded as "true" growth. Yet operationally, from the standpoint of quantitative *measurement* of growth of the organism as a whole, we must consider these non-protoplasmic inclusions—if they are irreversible—as parts of the growth process.



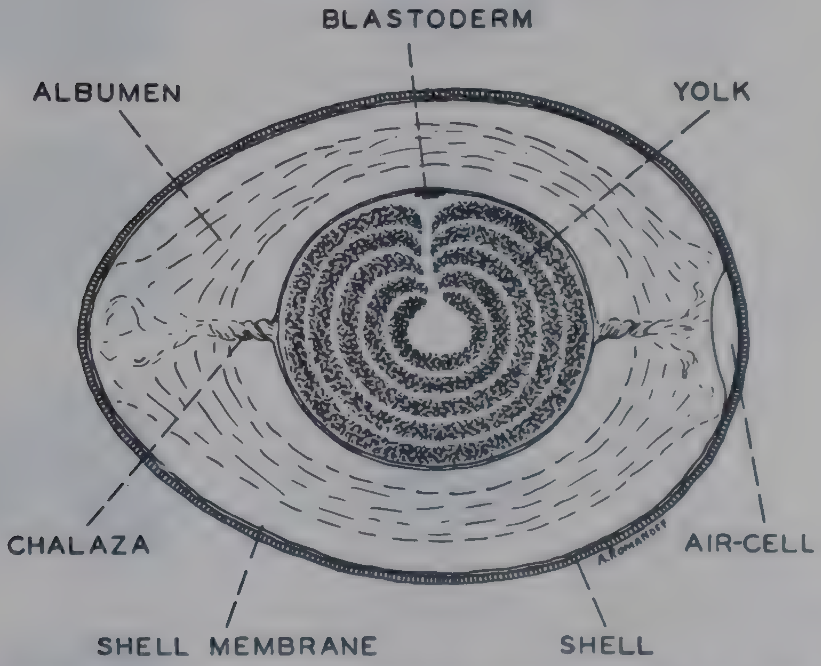


Fig. 16.3 a, b. Domestic fowl's egg and its development, from A. L. Romanoff, Cornell Exp. Bull. 205, 1931 and 1936. Beginning of alimentary tract, 18 hours; vertebral column, 20 hours; nervous system, 21 hours; head, 22 hours; blood island-vitellin circulation, 23 hours; eye, 24 hours; ear, 25 hours; heart beat, 42 hours; amnion, 50 hours; legs and wings 63 hours; allantois, 70 hours; reproductive organs, 5th day; feathers, 8th day; beak turns toward air cells, 17th day; yolk sac begins to enter body cavity, 19th day; yolk sac completely drawn into body cavity, 20th day; hatching of chick, 21st day.

The knowledge of the mechanism whereby the protoplasmic mass increases is in its initial stages of investigation[3] is not understood.

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[3] For literature see Gulick, A., *Growth*, **3**, 241 (1939); *Advances in Enzymology*, **4** (1944). Bergman, M., *Chem. Rev.*, **22**, 423 (1938). Wrinch, Dorothy, *Protoplasma*, **25**, 550 (1936); *Proc. Roy. Soc.*, **161A**, 505 (1937). Mark, H., *Nature*, **140**, 8 (1937). See also many papers by F. S. Hammett in *Growth* indicating the functions of various amino acids and other substances in growth of the hydroid *obelia;* Schoenheimer,[1] and Supplements 2, 3, and 4 (1940–42) to *Growth*.

Differentiation (cytogenesis, histogenesis) is transformation of mother cell, such as egg cell, into *different* kinds of daughter cells—brain cells, kidney cells, liver cells, etc. This process is irreversible. Egg cells are transformed to liver cells, but liver cells cannot be transformed into egg cells. There is a running down of growth potentialities with increasing differentiation in the individual, analogous to running down of free energy in the larger universe (Ch. 2).

Morphogenesis (organogenesis), another aspect of development, refers to the organization of the various cells into special organs of definite form, and the organization of the organ-systems into the body as a whole.

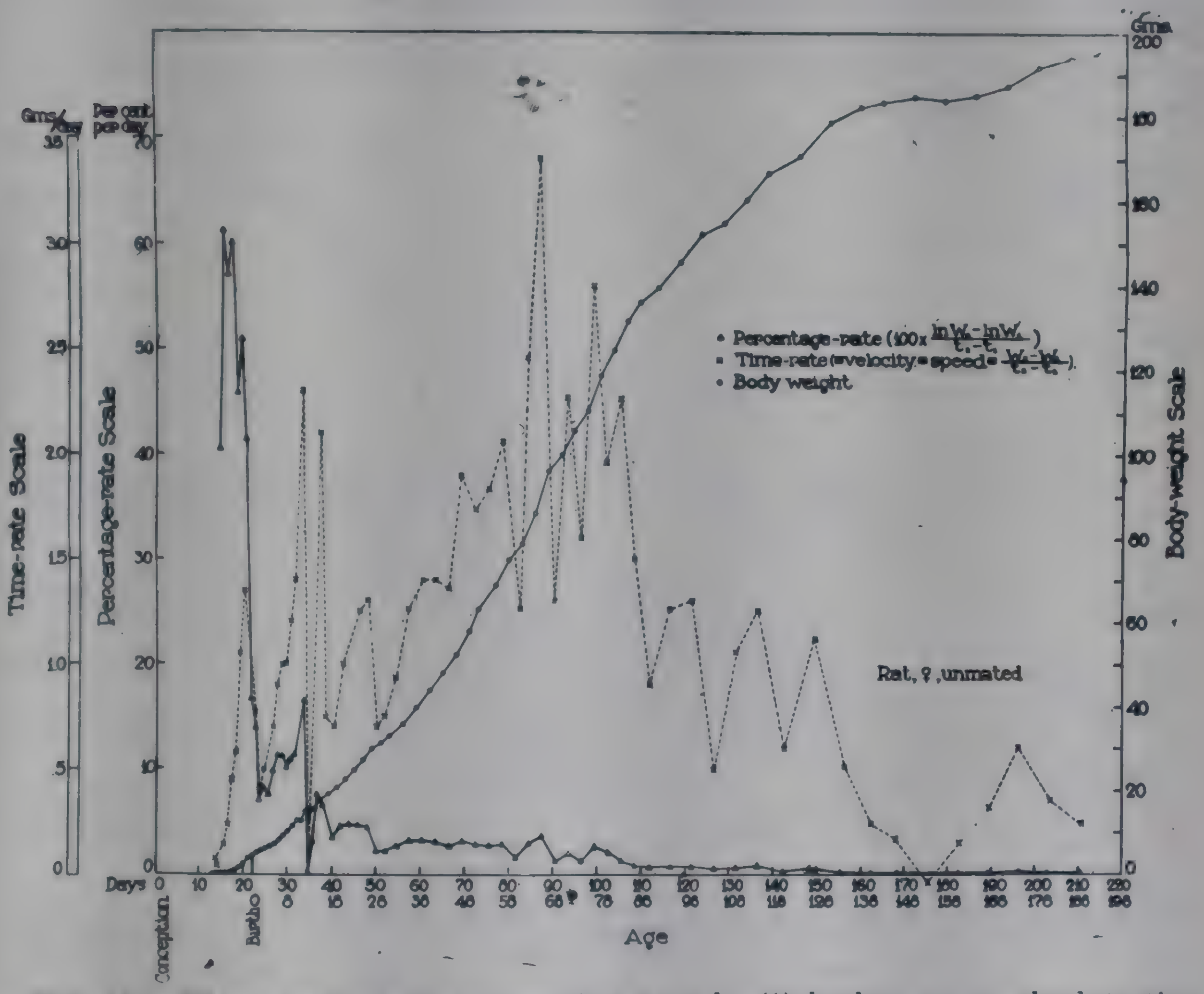

Fig. 16.4. Three methods of representing growth: (1) broken curve, absolute time gain; (2) declining curve with triangles, instantaneous percentage rate of growth $\left(100 \times \frac{1nW_2 - 1nW_1}{t_2 - t_1}\right)$; (3) rising S-shaped curve, cumulative or course of growth, or the total weight at given age.

Needham[4] subdivides *growth* into: (1) cell multiplication, (2) intussusception, or increase in size of cells, and (3) accretion or increase in amount of non-living structural matter; *differentiation* into: (1) increase in number of kinds of cells, and (2) increase in morphological heterogeneity; *metabolism* into: (1) respiration (oxidation), (2) fermentation or glycolysis, (3) catabolism of protein, (4) catabolism of fat, (5) chemical activity, as pigment-formation, glycogen synthesis, etc.

Other authors have other schemes of classifications. We defined development to include growth; Hammett defined growth to include development—growth is the coordinated expression of incremental and developmental factors and functions[5]. In this chapter, concerned not with growth mechanisms but with time relations, growth is defined operationally by increase in weight.

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[4] Needham, J., *Biol. Rev.*, **8**, 180 (1933).

The bird's egg is deceptively large because of its "cleidoic" nature[6], its yolk and albumen stores and related "redundant structures", such as air chambers for the nutrition of the embryo. In contrast, the mammalian egg is a minute speck. The mammalian egg, first observed in 1827 in the dog[7], appears to be nearly independent of the size of the mature animal. It ranges[8] from about 70 to 85μ (μ is $\frac{1}{1000}$ millimeter) in rodents (mice, rats, guinea pigs) to about 140μ in dogs, horses, sheep, goats, pigs, whales, and primates, including man. In other words, the egg of mouse, man, or whale is of practically the same size, about $\frac{1}{10}$ millimeter in diameter. Yet, a given egg grows, differentiates, and develops into chick, mouse, man, or whale and goes through life according to its respective inherited pattern.

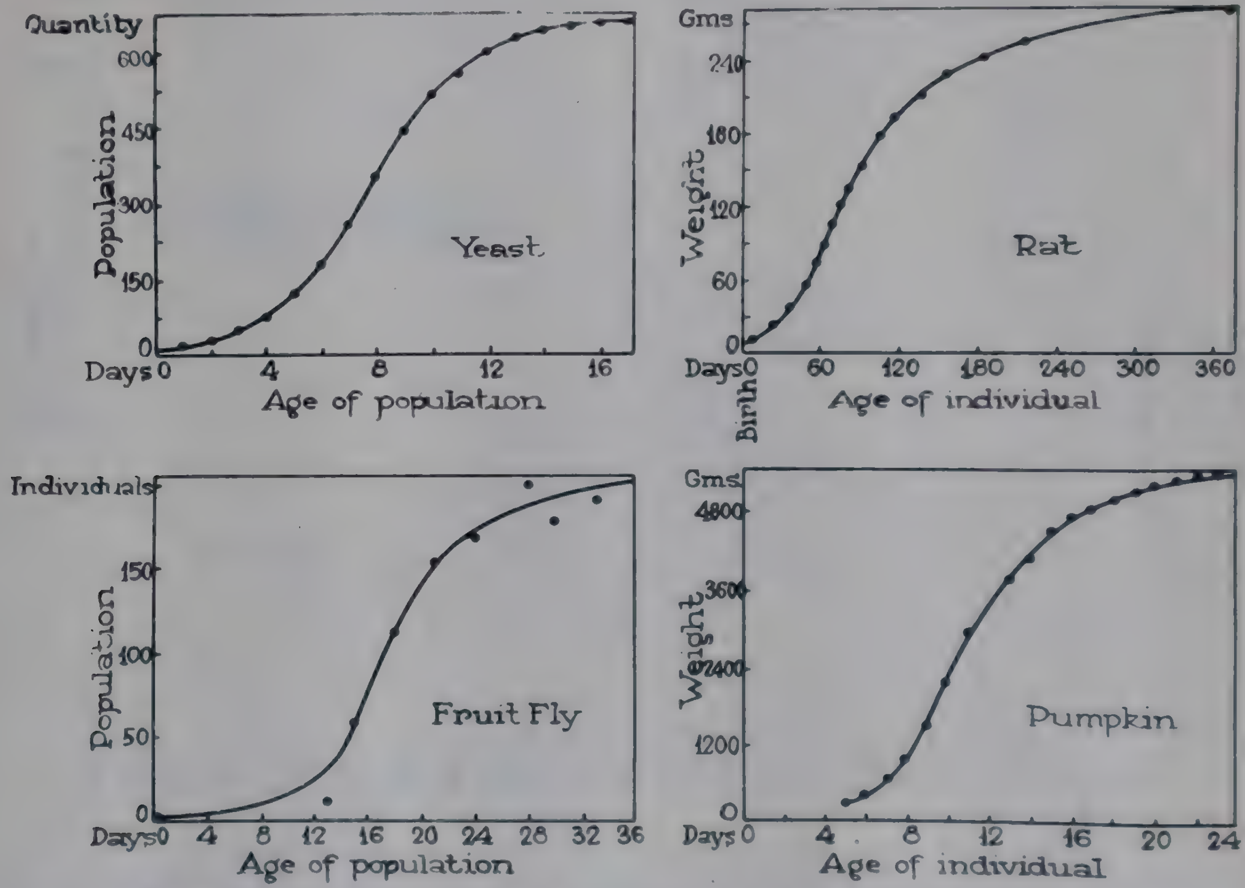

Fig. 16.5. Comparison of growth of populations and of individuals. For data and sources see R. Pearl, "The Biology of Population Growth," A. Knopf, N. Y., 1925.

The general appearance and cleavage of the egg of cow, pig, cat, muskrat, monkey, and man are similar[9, 10], as exemplified by Fig. 16.1 from Gregory[10] and Fig. 16.2 from various sources compiled by Pincus[11].

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[5] Hammett, F. S., "Nature of Growth," 1936; also many articles in *Growth*.

[6] Needham, J., *Chemical Embryology*, p. 1615.

[7] Von Baer, K. E., "Über Entwicklungsgeschichte der Tiere," 1828.

[8] Hartman, C. G., *Quart. Rev. Biol.*, **4**, 373 (1929).

[9] Streeter, G. L., *Sci. Monthly*, **32**, 495 (1931).

[10] For motion-picture photography of the egg and daughter cells, see Lewis, W. H., and Gregory, P. W., *Science*, **69**, 226 (1929); Lewis, *Anat. Rec.*, **48**, 52 (1931); Gregory, P. W., Carnegie Institution of Washington, Contributions to *Embryology*, **21**, 141 (1930); Squier, R. R., *Id.*, **23**, 225 (1932); Lewis and Hartman, C. G., *Id.*, **24**, 187 (1933); Lewis and Wright, E. S., *Id.*, **25**, 113 (1935).

[11] Pincus, G., "The eggs of mammals," Macmillan Co., 1936.

Under great magnification the fertilized mammal's egg is seen to contain particles in motion, in agitation, eventuating in cleavage of the egg cell into two daughter cells. In this division, as in perhaps the following 3 or 4 cleavages, there is no increase in the mass as a whole, but only subdivisions of the cells.

This basic process of division of one cell into two, the nature of which is not understood, is one of the most distinguishing characteristics of living organisms. An even more remarkable example of division, inexplicable by known physical forces, is the production and expulsion of polar bodies by the unfertilized egg in preparation for the reception of the sperm's contribution to the *zygote*[12]. This "anticipation" of future developmental needs of both the individual and the race sets living processes apart from non-living. Similarly, other structures develop in anticipation of—and long before—the time when they will be called upon to function in the service of the organism as a whole (Ch. 10).

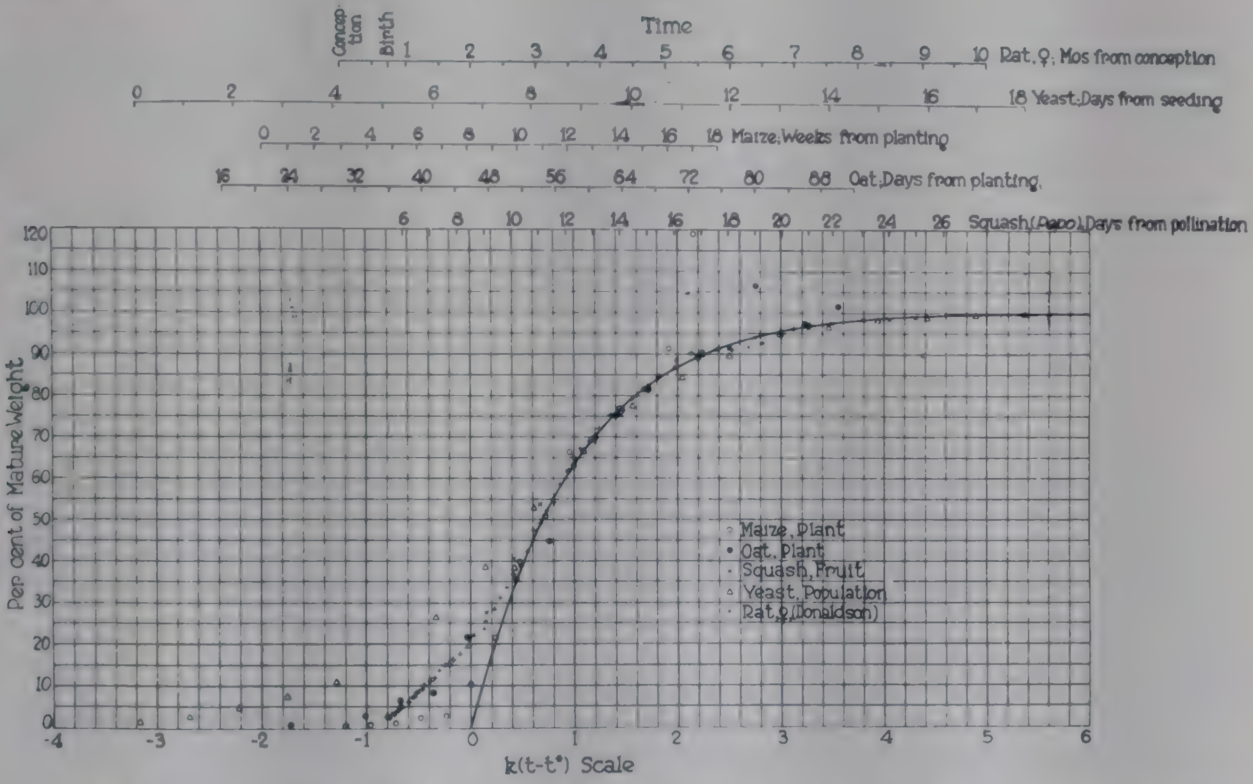

Fig. 16.6. Equivalent growth curves of rats, yeast populations, maize plant, oat plant, and a squash.

There is no pronounced increase in the size of the mass in the first few cleavages of the fertilized egg, but there is increasingly pronounced differentiation so that at the 16-cell stage the *trophoblasts*, the cells destined to furnish the fetal membrane, and the structures of implantation of the egg on the maternal tissue, become distinctive. The trophoblast cells divide more rapidly and are, therefore, smaller than the other cells.

Next most conspicuous is the formation of the fluid-distended vesicle, the *blastocyst* (Fig. 16.1), and cupping into a hollow sphere. Fluid collects within this sphere, perhaps through the secretory activity of the trophoblast cells, and the cell mass, for the first time, enlarges by the accumulation of fluids.

The outstanding feature of the "growth" of the blastocyst is the absorption of tremendous quantities of water. Davenport[13] estimated that after six weeks the human egg is nearly 500,000 times its initial weight, weighing about a gram, the increase in weight being 98 per cent water. Water is economical for growth and gives plenty of "elbow room" for the developmental processes; it is the solvent and carrier of nutrients and wastes, and there must be plenty of it prior to the development of the circulatory system.

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[12] Zygote, the "yoked" first cell of the body, the union of male and female germ cells, or gametes, carriers of the genes or hereditary determiners.

[13] Davenport, C. B., "How we came by our bodies," New York, 1936.

The blastocyst forms the embryonic envelope and establishes contact for the interchange of fluids between embryo and mother. After the attachment of the egg, the inner cells begin segmentation and differentiation to form the embryo and the amniotic and yolk-sac vesicles form. The two vesicles flatten against each other and, together with the cells between them (mesoblast cells), form a three-layered germ disk which forms the embryo. The remainder is, like the trophoblast, accessory and temporary. The germ disk is formed in man about the third week.

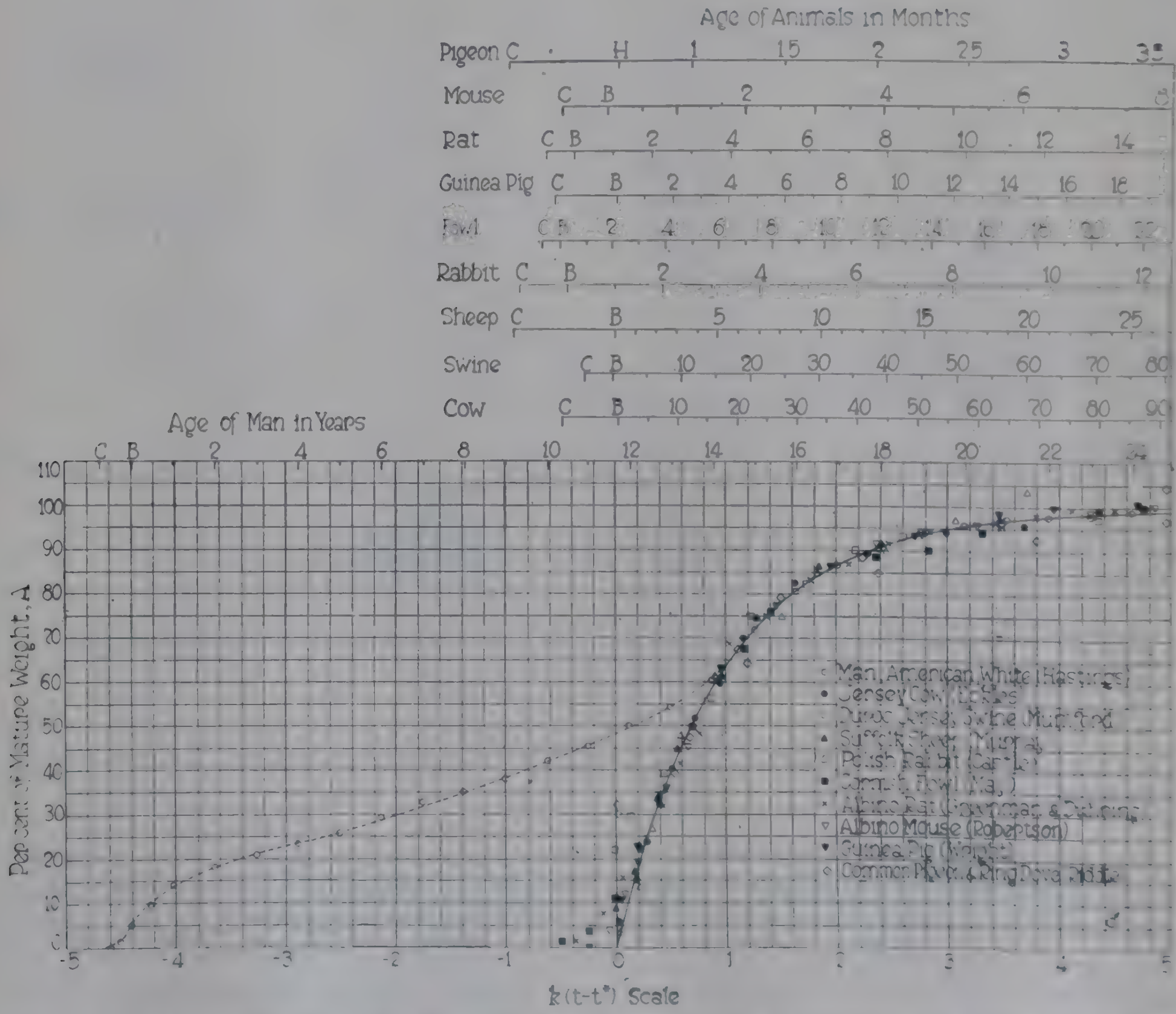

Fig. 16.7. Weight-growth equivalence of farm animals, laboratory animals, and man.

The cupping in of the amniotic and yolk-sac vesicles to form the germ disk is mechanically somewhat analogous to the cupping in of the two walls of a hollow rubber ball, and is in a way characteristic of the successive infoldings during organ formation.

The layers interact in the production of new kinds of cells, the segregation and differentiation of which eventuate in organ formation (Fig. 16.3). In man, the external features of the embryo are easily recognizable as distinctively human by the latter part of the second month. Eyes, mouth region, and limb buds may be recognized by the fourth week in man, and the organs are formed by the third month. In other words, the "ground plan" is laid very early in life and rounded out later through enlargement and remodeling of the parts. Age changes in shape are due to differences in growth rates of the constituent parts (Ch. 17).

There is an orderly sequence, or *gradient*[14], in organ formation. The head has precedence in development over the tail end, and so on in cephalochordal sequence for the other organs. The sequences may be associated with organizer and hormone action (Ch. 7).

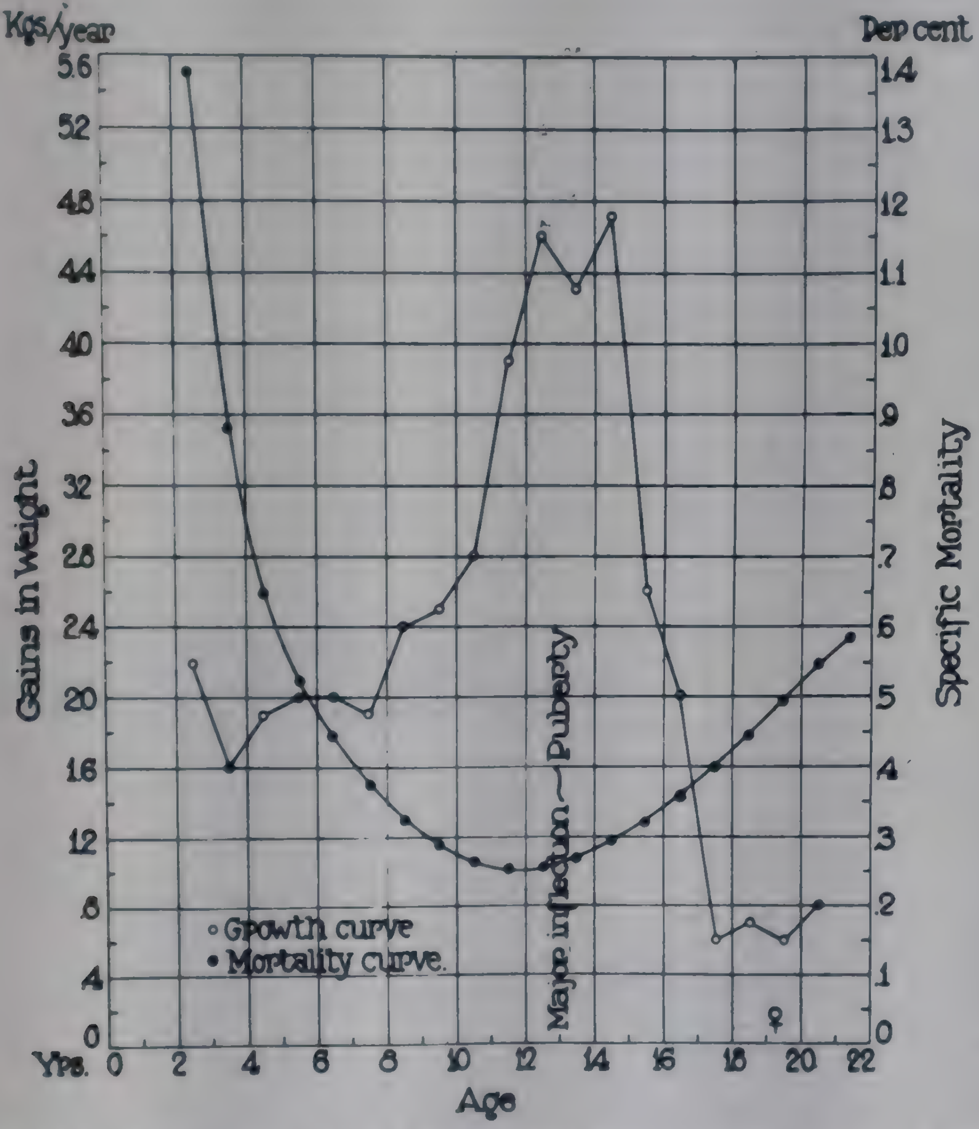

Fig. 16.8. Comparison of weight gain and specific mortality in children.

With these brief definitions and introduction we proceed with our major problem, an analysis of the time relations of growth in weight.

Many of our gigantic industrial organizations are extremely complex; no one can know all their details. Yet accountants, quite ignorant of these details, render intelligible and useful corporate statements. Likewise,[15] the animal body is extremely complex; no one can know all its details. Yet, as we shall show in this chapter, the time relations of growth can be represented by intelligible, useful, and rational statements or "laws" of growth.

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[14] *Cf.*, Child, C. M., "Individuality in organisms," Univ. Chicago Press, 1915.

[15] *Cf.* Bertalanffy, L. V., "Theoretische Biologie, Berlin," 1932; also *Roux Arch.*, **131**, 613 (1934), and *Human Biology*, **10**, 181 (1938).

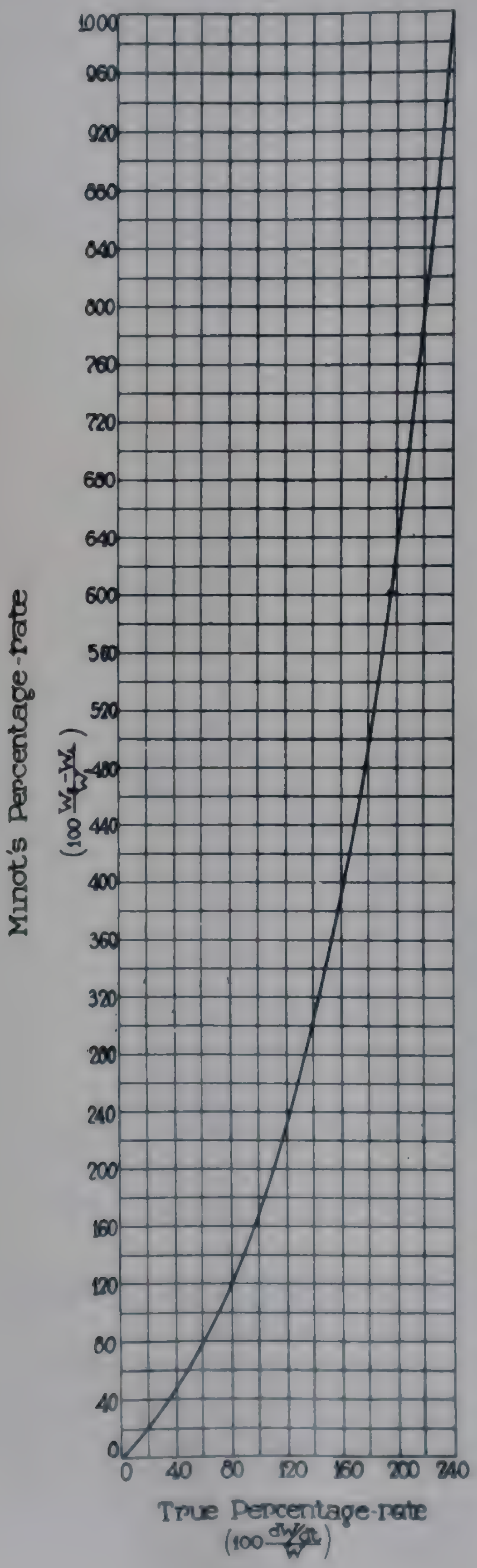

Fig. 16.9. The relation between the percentage growth rate computed by the instantaneous logarithmic and by the finite arithmetic method.

It may be recalled in this connection, that some of the great laws of the physical sciences, such as Newton's law of gravitation, say nothing about detailed mechanisms involved; they are only intelligible, useful, and more or less rational descriptive statements of the phenomenon. There is, of course, a wide range in rationality in many so-called "laws" of nature. We hope that the following growth equations partake more of laws of nature and less of the accountant's purely empirical rendering of a financial statement.

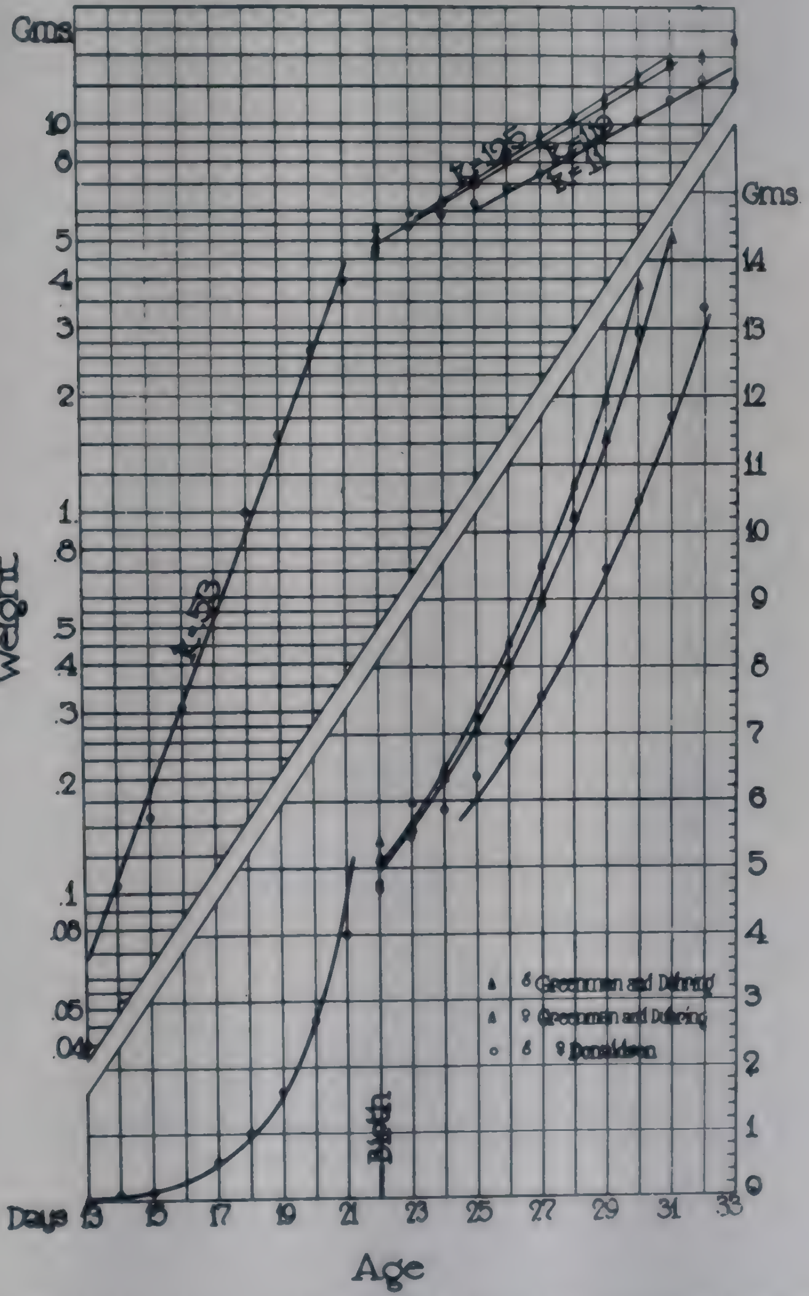

Fig. 16.10. Growth of the white rat between 13 days after conception and 10 days after birth, plotted on arithlog and on arithmetic coordinate paper.

16.2: The shape of the age curve of growth of individuals and populations

> There is no bound to prolific nature in plants and animals but what is made by their crowding and interfering with each other's means of subsistence. *T. R. Malthus* (1798)

Fig. 16.5 represents age curves of growth of *populations* of yeast and flies, and of *individual* pumpkins and rats. They all have the same s-like shape. Indeed, all these curves may be made to coincide, as shown in Fig. 16.6. Fig. 16.7 demonstrates the close similarity between the age curves of different animal species. The human age curve, however, differs from the others in having a very long juvenile period, a long interval between weaning and puberty (approximately 3 to 13 years); this period is almost absent in laboratory and farm animals. In these animals, weaning merges into adolescence without the intervention of the juvenile phase found in man. The uniquely long juvenile period in man should be of particular interest to students of education.[16]

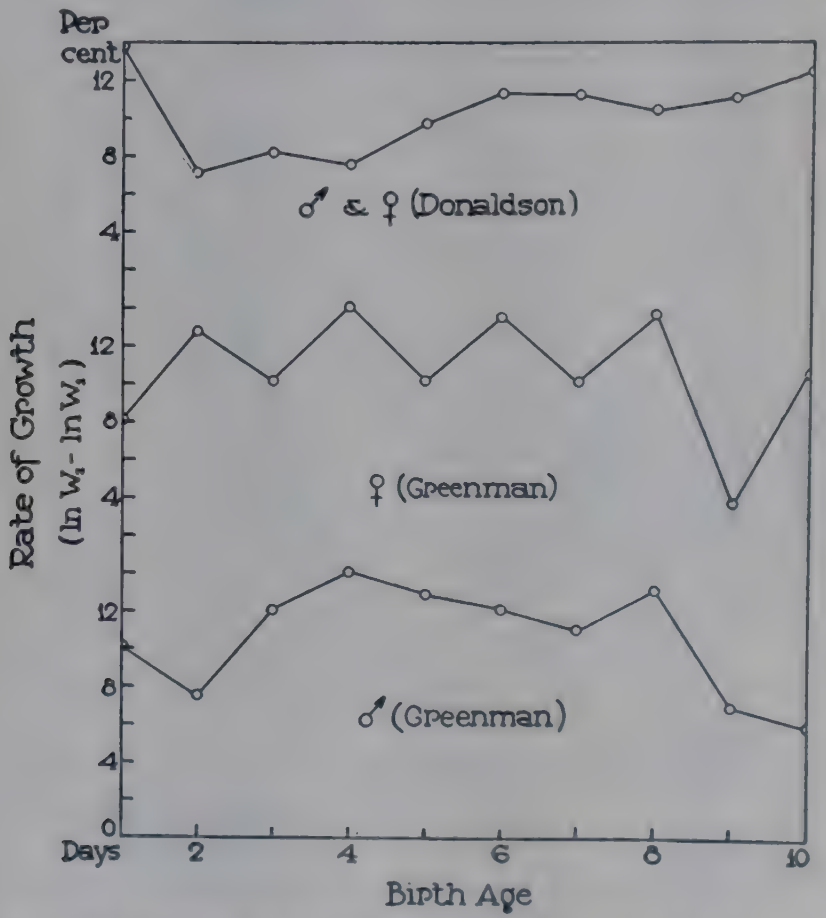

Fig. 16.11. The true percentage growth rate of three sets of rats during the first ten days of postnatal life.

The general similarity between the curves of growth of individuals and of populations is not surprising, since ultimately both are collections of individuals. Our bodies are made of cells, and our bodies, in turn, are cells in the social body. Individuals are organisms and also units of a larger organism, an epiorganism (Sect. 10.9).

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[16] *Cf.* Fiske, John, in "The Meaning of Infancy"; Boston, 1883: "If there is any one thing in which the human race is signally distinguished from other mammals, it is the enormous duration of their infancy . . . this period of helplessness . . . is a period of plasticity . . . a door through which the capacity for progress can enter . . . power to modify . . . inherited tendencies."

It may be seen from Fig. 16.4 that the age curve of growth may be divided into two principal segments, the first of increasing slope, which may be designated as the *self-accelerating phase of growth*, and the second of decreasing slope, which may be designated as the *self-inhibiting phase of growth.*

The general shape of the age curve may thus be said to be determined by two opposing forces: *a growth-accelerating force* and *a growth-retarding force.* The former manifests itself in the tendency of the reproducing units *to reproduce at a constant percentage rate indefinitely, when permitted to do so. In the absence of inhibiting forces*, the number of new individuals produced per unit time is always proportional to the number of reproducing units. That is, the *percentage* growth rate *tends* to remain constant. The potentially infinite growth ability and consequent immortality of somatic cells was established by Leo Loeb[17] by *in vivo* experiments with cancer tissue (trans-

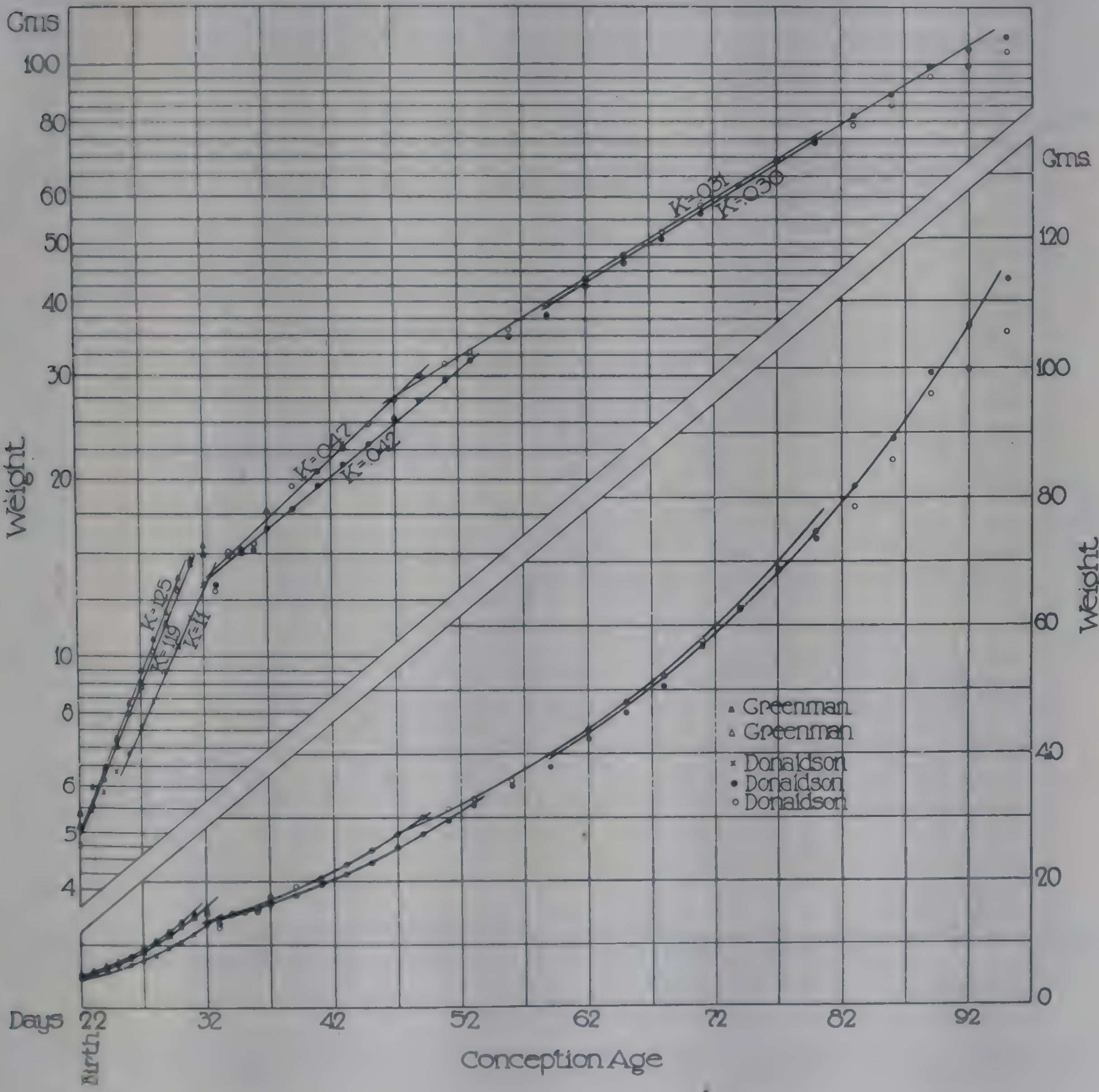

Fig. 16.12. Postnatal growth of rat to the pubertal inflection

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[17] Loeb, L., *J. Med. Res.*, **6**, 28 (1901), and *J. Gen. Physiol.*, **8**, 417 (1926).

plantation of the cancer tissue to successive generations of animals), and verified by Carrel[18] by *in vitro* experiments with normal connective and other tissues, by cultivating tissue cells *in vitro* under conditions of continuous irrigation, thus preventing change in environment which would result in the development of growth-inhibiting forces.

But there comes a time, marked especially by the inflection in the growth curve, when the increase in the population tends to be proportional not to the number of reproducing individuals in the population but to the available resources necessary for growth; the resources may be in the form of space, food, freedom from the encroaching by-product of growth, as lactic acid in the case of growth of lactic acid bacteria in milk. It is the environment—or the growth-inhibiting force in the environment—which exerts the limiting influence on growth after the inflection in the curve.

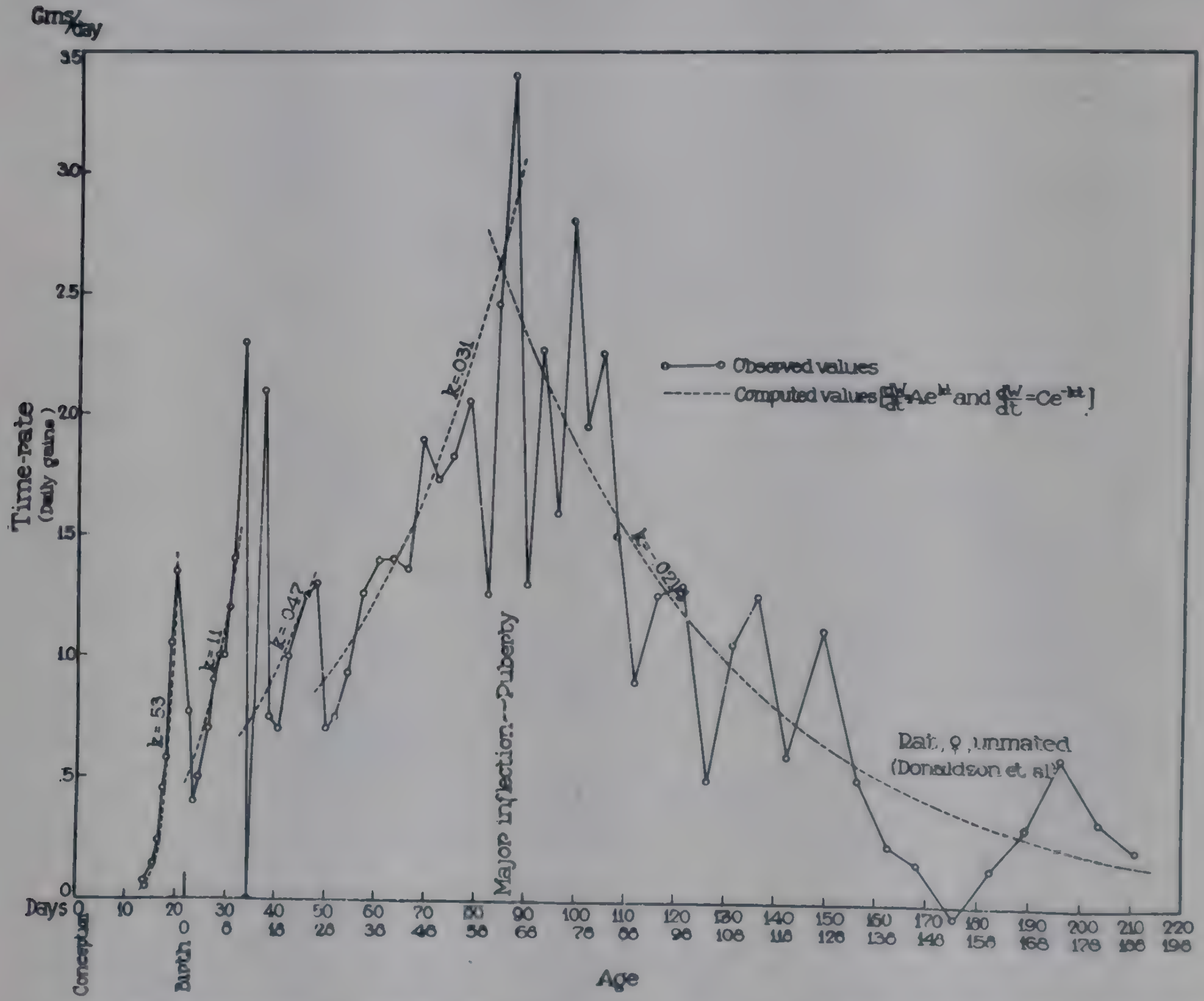

Fig. 16.13. Illustration of the discontinuous nature of the growth process by the daily weight increments, and the fit of the equation (16.6) to the increment curves.

And so, with the passage of time, the growth-inhibiting force or forces develop, counteracting and finally bringing the growth process to a virtual standstill.

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[18] Carrel, A., *J. Exp. Med.*, **38**, 521 (1933). Carrel and Ebeling, A. H., *Id.*, **34**, 317 and 599 (1921).

The inflection in the age curve (Figs. 16.4 to 16.8 and 16.13) represents the position at which the increase in growth velocity ceases, and the decrease in velocity has not yet begun; therefore, the inflection represents the position at which gains are most rapid, and perhaps most economical (Figs. 16.4 and 16.8).

At the point of inflection the *change* in the time rate of growth (*i.e.*, in acceleration) is the same in all animals or populations (the numerical value of the acceleration at this time is zero). This is, therefore, a point of geometric and physiologic age equivalence. There is at least one physiological stage through which all animals seem to pass at this time, *i.e.*, puberty. Thus in Fig. 16.4 the inflection in the curve of the female rat occurs at about 65 days (86 days after conception), and this is the usual age at which the vagina opens. In children the inflection occurs between 12 and 15 years, the age of puberty.

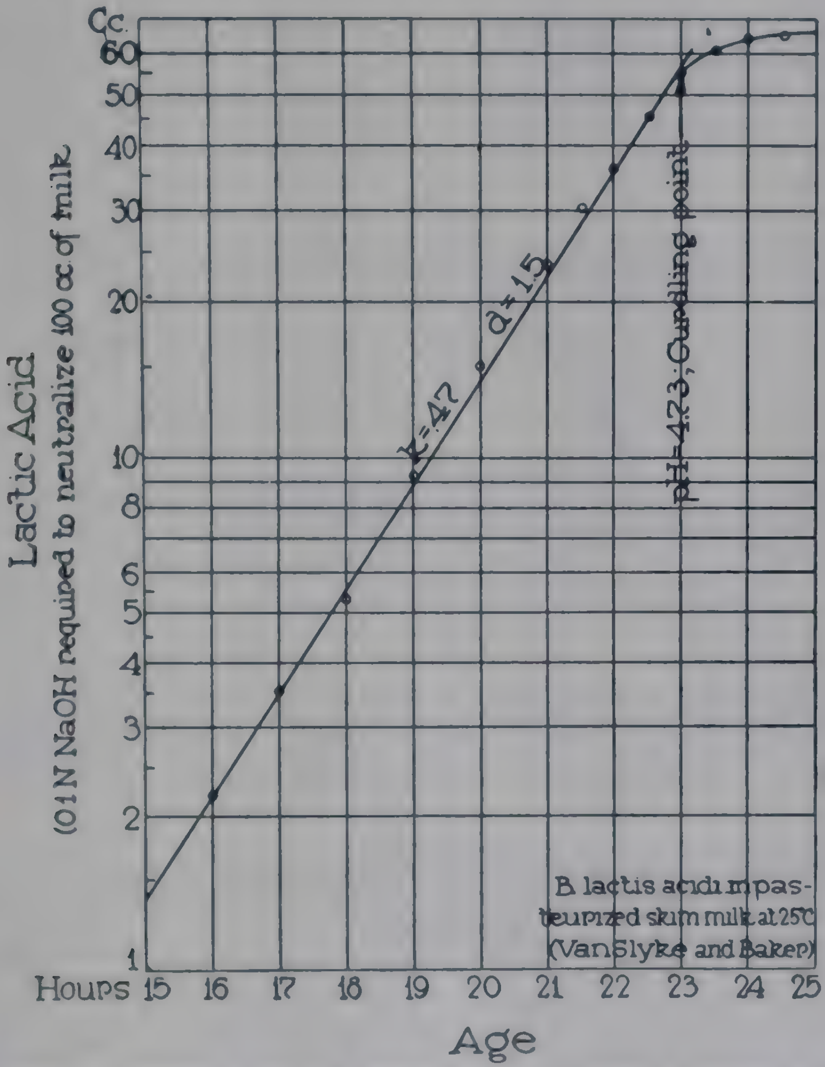

Fig. 16.14. The percentage rate of growth of lactic-acid bacteria is constant until pH 4.73 is reached. The acid increases at 47 per cent per hour, or is doubled in $\frac{0.69}{0.47} =$ 1.5 hours.

A third fact relating to children, and possibly to animals also, is that the curve of specific mortality (*i.e.*, the ratio of the number dying to the number living *of the same age*) passes through a minimum at approximately the same age as the growth curve passes through its inflection. This is shown in Fig. 16.8. The specific mortality decreases to this age, and increases thereafter.

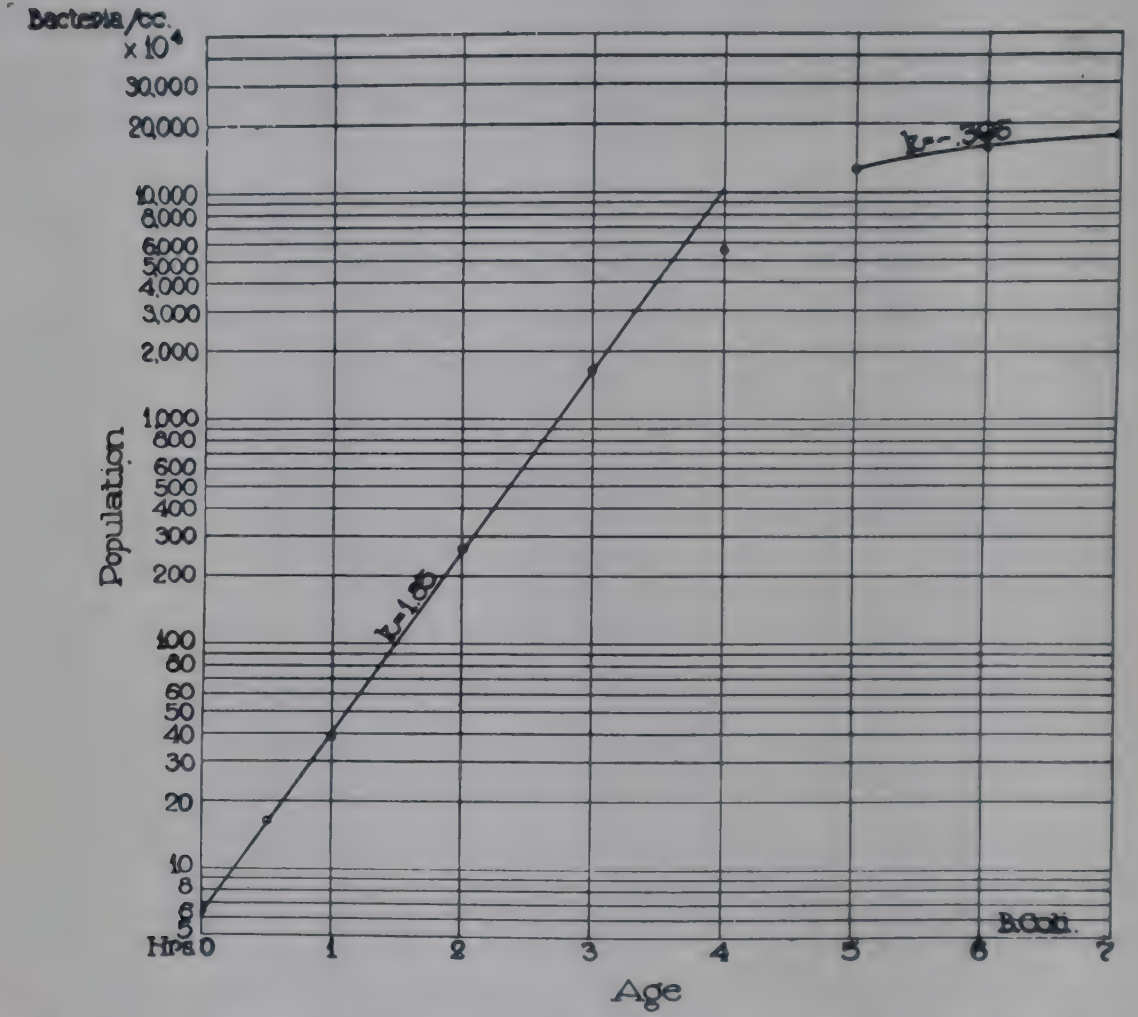

Fig. 16.15. Growth of *B. coli* at 37°C. in a given volume of broth [Exp. 7, McKendrick and Pai, *Proc. Roy. Soc. Edinburgh*, **31,** 649 (1911)]. As $k = 1.85$, growth was at 185 per cent an hour; the population is doubled in $\frac{0.693}{0.185} = 0.37$ hour, or 22.2 minutes.

The point of inflection, then indicates: (1) the time of maximum velocity of growth (transition from increasing to decreasing growth velocity); (2) the age of puberty; (3) the lowest specific mortality, the beginning of the period of increasing specific mortality; and (4) a geometric referent for the determination of equivalence of age in different animals (and also equivalence of age in the growth of populations). The point of inflection is thus an important growth constant. Figs. 16.7 and 16.8 show that the inflection in man occurs at the age of about 14, which corresponds on the axis of ordinates to somewhat over 60 per cent of the mature weight. In chimpanzees the inflection (at age seven years) occurs at slightly below 60 per cent of the mature body weight.[19] In laboratory and farm animals (Fig. 16.7), on the other hand, the inflection takes place when about 30 per cent of the mature weight is reached, corresponding to about six months in cattle, or two months in sheep.

Summarizing, the shape of all age curves of growth, whether of individuals or populations, is sigmoid; the early phase is of rising slope and the later phase of declining slope. The junction between the two phases occurs during puberty in animals, flowering in plants, and "coming of age" in populations, when, because of the back pressure of the environment, the reproductive rate declines or the excess population sets out on migrations, such as the dramatic migration of the lemming to the sea.

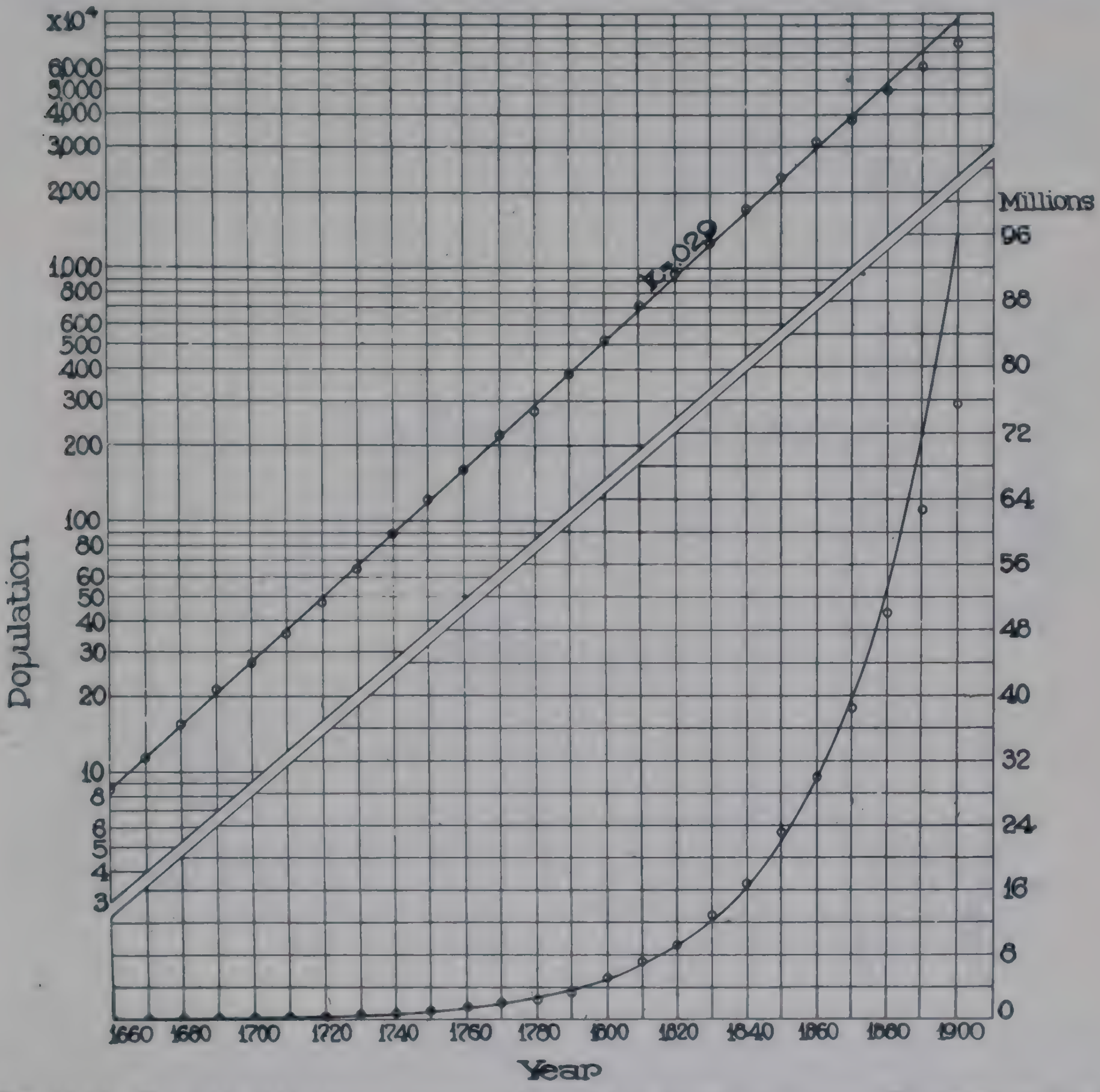

Fig. 16.16. Growth of the human population in the North American Colonies and in the United States. $k = .029$; the population increased at 2.9 per cent per year, doubled itself in $\frac{0.693}{0.029} = 24$ years. (From data in "A century of population growth in the United States" by W. S. Rossiter, Bureau of the Census, United States Department of Commerce and Labor, Washington, 1909).

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[19] Grether, W. F., and Yerkes, R. M., *Am. J. Phys. Anthrop.*, **27**, 181 (1940).

16.3: Definitions and quantitative representations of growth rates

> If nature were our banker, she would not add the interest to the principal every year; rather would the interest be added to the capital continuously from moment to moment. *J. W. Mellor*

For purposes of *quantitative* analysis, growth may be defined as relatively *irreversible* time change in magnitude of the measured dimension or function.

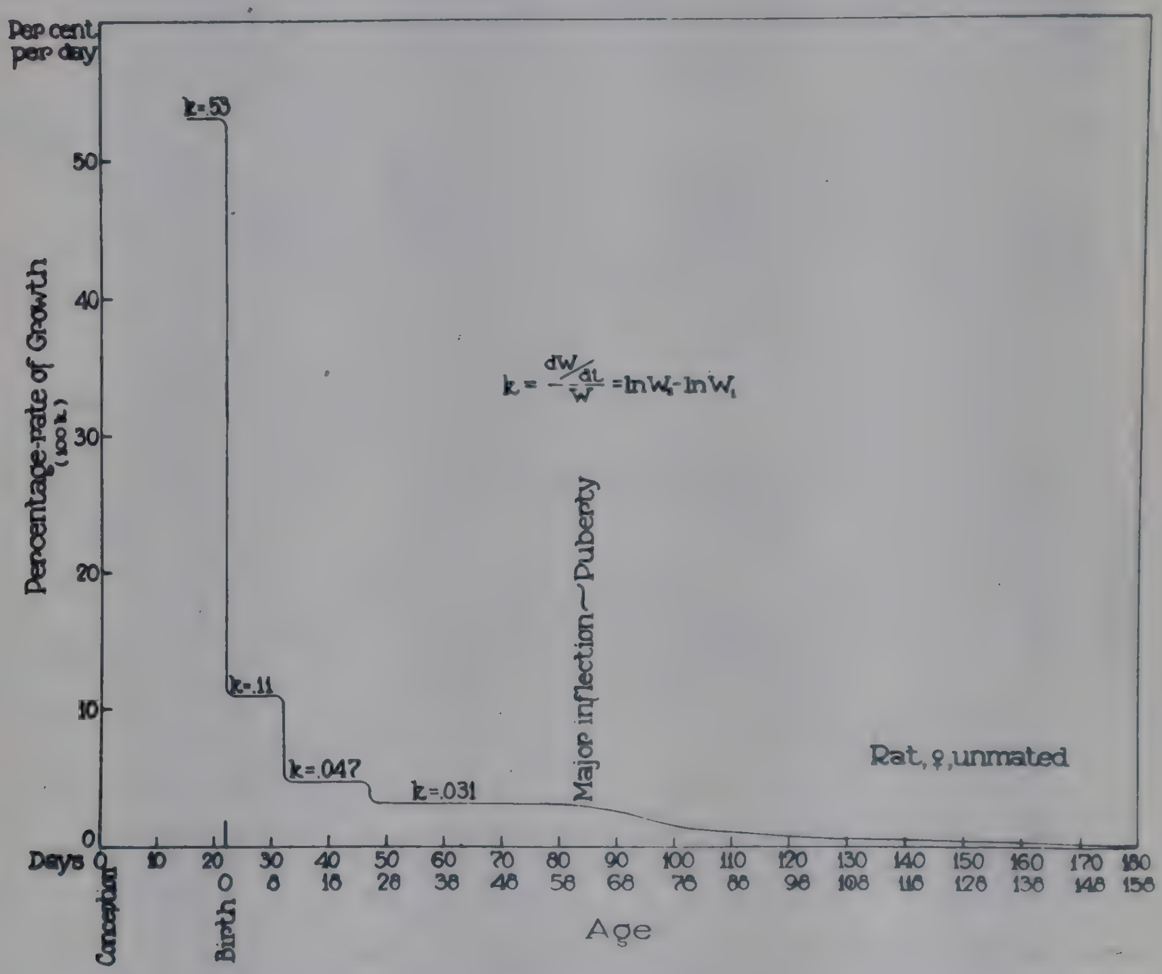

Fig. 16.17. The percentage rates (100k) of growth of the albino rat plotted against age. These are, of course, computed values, computed by the graphic method explained in the text. The curve illustrates in a striking manner the discontinuous nature of the growth process.

The concept of irreversibility is emphasized to exclude fluctuating time changes of a fortuitous nature, such as those occasioned by fluctuating food supply with consequent fattening and leaning, with gestation, lactation, and so on.

Growth in weight is usually represented in one or all of the three ways shown in Fig. 16.4: (1) *absolute* gain in the given magnitude per unit time; (2) *relative* rate (or *percentage* when multiplied by 100) gain per unit time; (3) *cumulative*, or course-of-growth weight up to, or the weight at, a given time. All these forms of representation may be made in conventional mathematical terminology.

Thus the absolute gain in the observed-weight difference, $W_2 - W_1$, for the corresponding time difference, $t_2 - t_1$, may be represented by the equation

$$\text{Average } \textit{absolute} \text{ growth rate} = \frac{W_2 - W_1}{t_2 - t_1} = \frac{\text{larger weight less smaller weight}^{20}}{\text{larger time less smaller time}} \qquad (1)$$

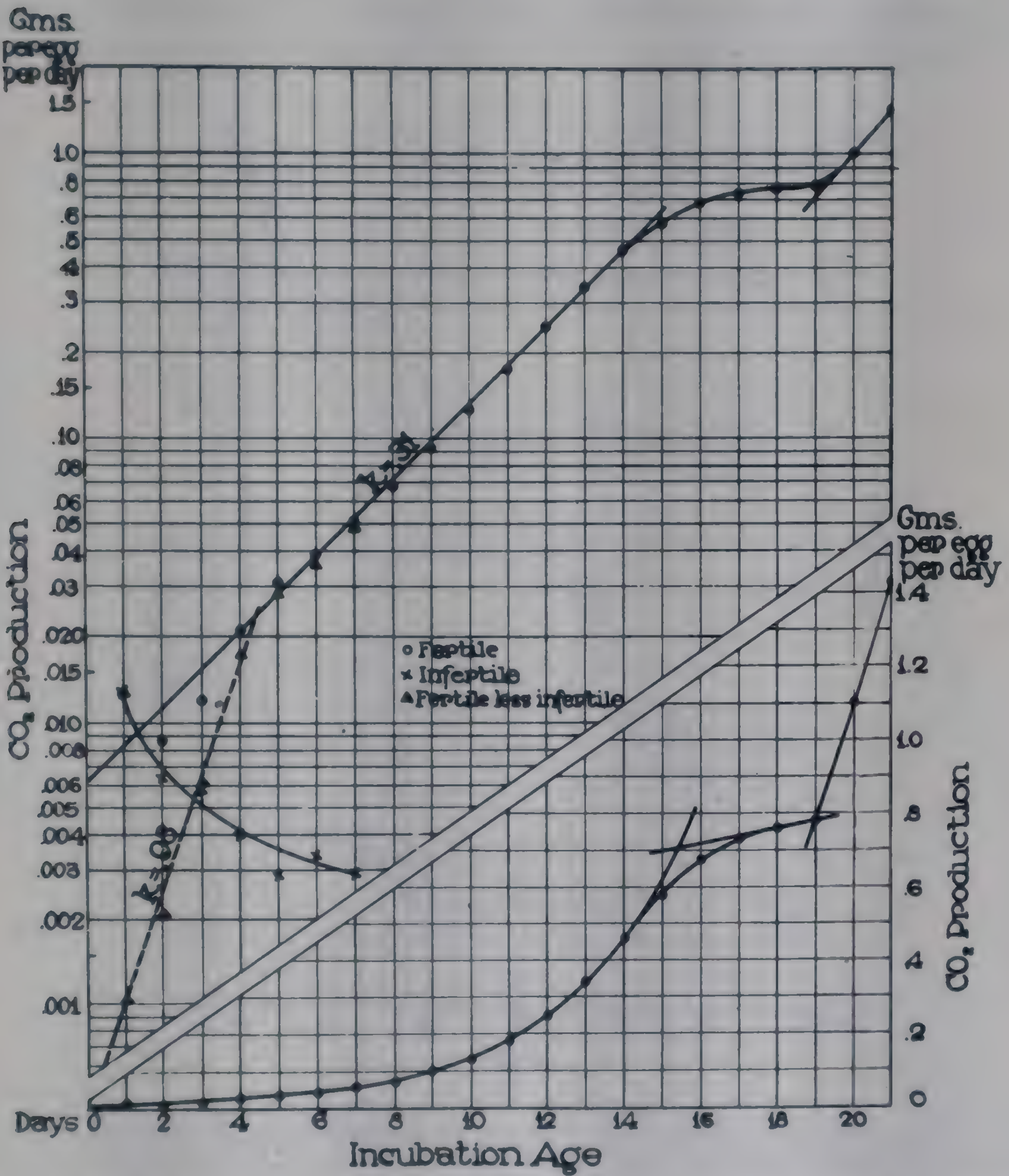

Fig. 16.18a. Carbon dioxide excretion in the chick embryo. From 0 to 4 days the rate of increase is 98 per cent per day (doubled once in 0.7 day or in 17 hours); between 4 and 14 days, the rate is 31 per cent per day (doubled in 2.2 days). The pause in the curve coincides with the maximum in the mortality curve (Fig. 16.20), and with the change in the mode of respiration (see text).

Equation (1) represents *average* absolute growth rate, in contrast to *true* growth rate applicable to extremely short intervals of time only. If a Holstein cow weighs 1000 pounds at age 1000 days from conception, she gained *on the average* one pound a day; but there was no day when she actually gained

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[20] *Cf.* Hayes, F. R., and Armstrong, F. H., *Can. J. Res.*, **21**, 23 (1943).

exactly one pound. To cite extreme illustrations, at the end of the first week after conception, she gained only about 0.0001 pound a day; at 5 months after birth, 2 pounds a day; at 1000 days, only one-fourth a day. Thus the concept of *average rate*, when applied to growth, is an abstraction, and when the average extends over a considerable period of time, as in the example cited, it gives no idea of the actual rate at any given age. The shorter the interval of time for which the average is computed, the more nearly does it approach

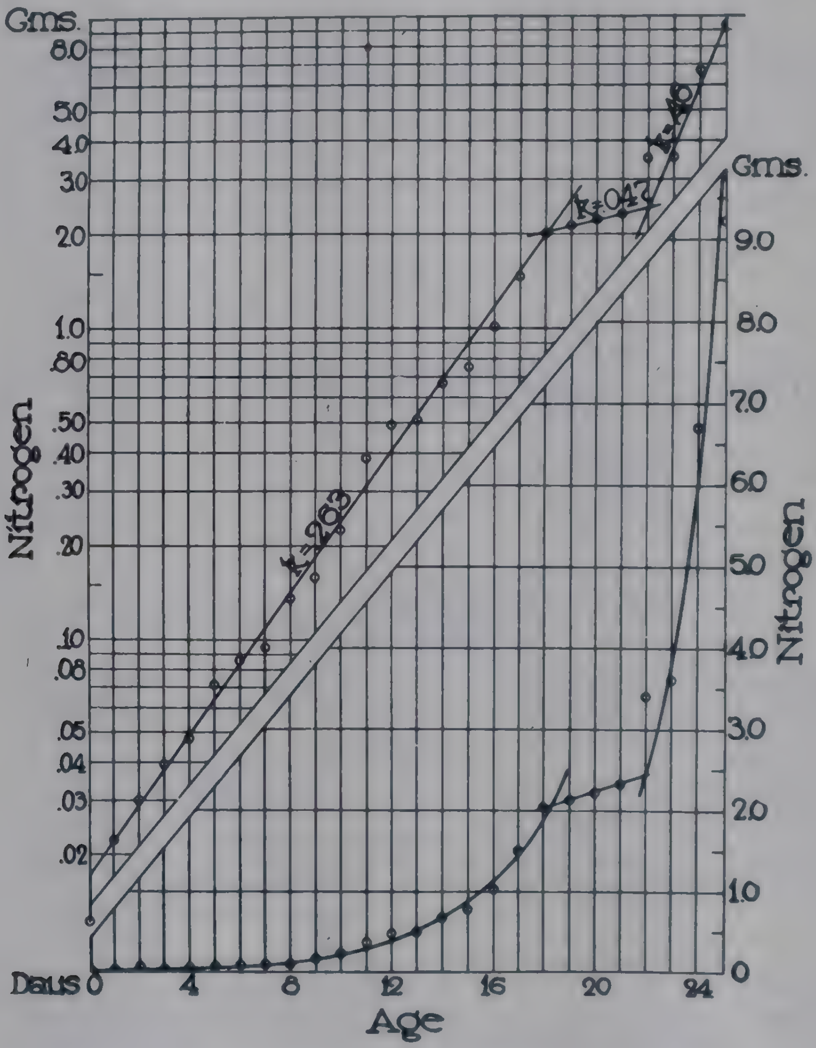

Fig. 16.18b. Nitrogen storage in the silk worm, from data by Luciani and Lo Monaco. The nitrogen curve of the silk worm embryo is similar to the CO_2 excretion curve of the chick embryo.

the true value; and when reduced to an interval, *dt*, so short that there is no time for the velocity of growth to change, the true growth rate, dW/dt, is obtained. *True* growth rate is then *instantaneous* growth rate, dW/dt.

Similarly, *relative* (or when multiplied by 100, *percentage*) growth rate is conventionally represented by the weight gain during a given time interval divided by the weight of the organism, W_1, at the *beginning* of the time interval:

$$\text{Average } \textit{relative} \text{ growth rate, } R = \frac{W_2 - W_1}{W_1} \tag{2}$$

Here again we have not *true* or *instantaneous* growth rate, but the conventional (Minot's) growth rate. The conventional and true percentage growth rates are nearly identical when the weight gain, $W_2 - W_1$, is very small *in comparison* to the weight of the organism. But when the weight gain is relatively

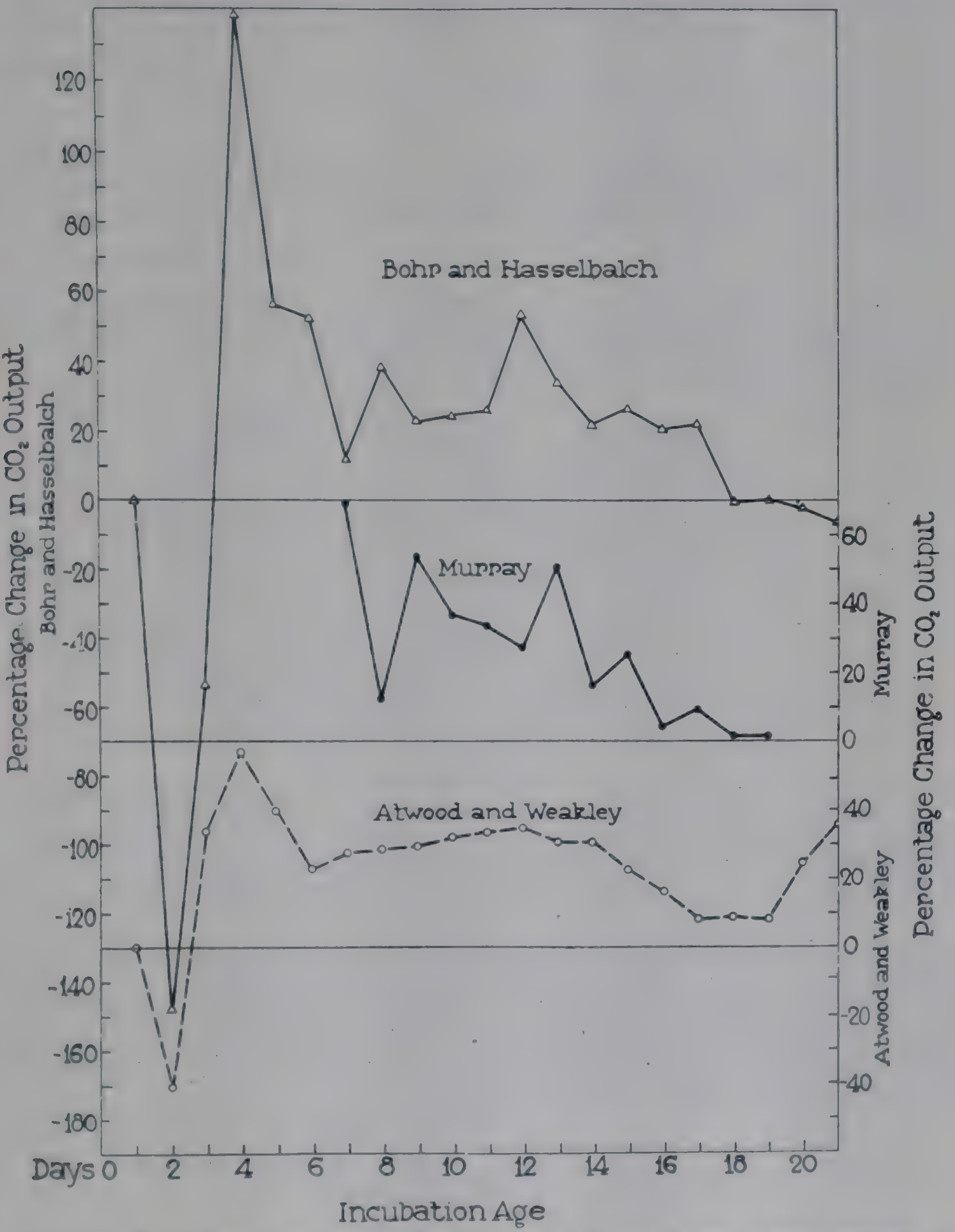

Fig. 16.19. Carbon dioxide excretion in the chick embryo, from three sources. The percentage rates were obtained by subtracting the natural logarithms of the successive values, and multiplying the result by 100. The fluctuations between 4 and 14 days are slight and there is no systematic change in the rate.

large compared with the body weight, the conventional growth rate computed from equation (2) may be misleadingly exaggerated, because the weight at the beginning of the time interval, W_1, existed a relatively long time ago, not *at* the time of observation. Thus the computed percentage growth rate of the population in this country would be enormously exaggerated if the population gain from 1666 to 1940 were related to the population size in 1666. The population gain during 1940 must be related to the population size during 1940, not during 1666. Likewise, the relative growth rate of an animal *at* a given age must properly be related to the body size *at* the given age, not the body size, W_1, of some earlier age, t_1.

Another objection to Minot's equation (2) for computing percentage rate is its failure to recognize that the *physiologic* significance of a physical unit of time, such as a day, changes rapidly with age. The growth rates computed by equation (2) are for continuously decreasing *physiological* time intervals, even though they are for constant astronomic or *physical* time intervals. The use of instantaneous rates eliminates the discrepancy between *physiologic* and *physical* time (Ch. 19).

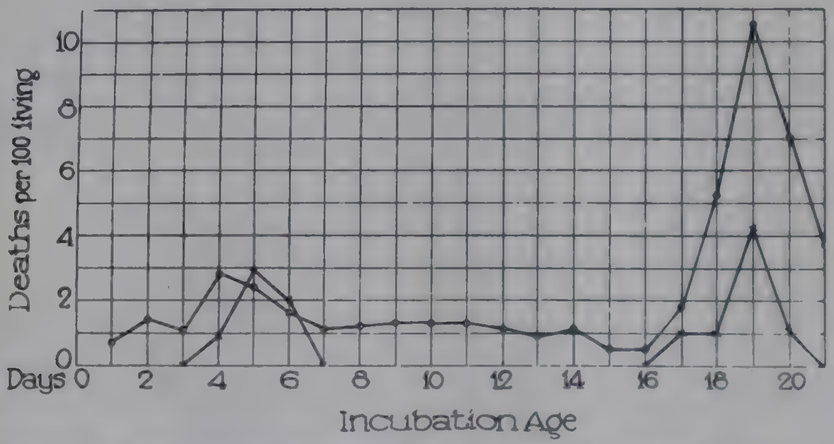

Fig. 16.20. Percentage mortality in the chick embryo. Circles represent embryos in an incubator; crosses, incubation under hens. The first peak in the mortality curve corresponds to the peak in concentration of lactic acid as reported by Tomita. The second peak in the mortality curve coincides approximately with the pause in the growth curves.

A more appropriate denominator would be the *average* weight of the organism during the time of observation. Thus if the weights of the organism at the beginning and at the end of the interval are respectively W_1 and W_2, then the average weight during the interval is $\frac{1}{2}(W_2 + W_1)$. Replacing W_1 in equation (2) by $\frac{1}{2}(W_2 + W_1)$, we obtain

$$\text{Average } \textit{relative} \text{ growth rate} = \frac{W_2 - W_1}{\frac{1}{2}(W_2 + W_1)} \tag{3}$$

Although equation (3) is an improvement over equation (2), it is still physiologically unsatisfactory because (1) the time intervals, $t_2 - t_1$, are arbitrary and not equivalent physiologically for successive stages of development; (2) the weight increments are assumed by this method to be added on at discontinuous time intervals; (3) the denominator, $\frac{1}{2}(W_2 + W_1)$, is obtained on the assumption that the growth rate occurs in a linear manner, which in practice is true only for short intervals.

In place of finite weight gain, $\dfrac{W_2 - W_1}{t_2 - t_1}$, we use "instantaneous" weight gain, dW/dt, and divide the "instantaneous" gain by the weight at the time of the gain, thus:

$$\text{Instantaneous (true) relative growth rate} = \frac{dW/dt}{W} \tag{4}$$

In this case, the denominator, W, represents the weight of the animal *at* the instant the rate dW/dt is measured, not the weight, W_1, at some earlier age.

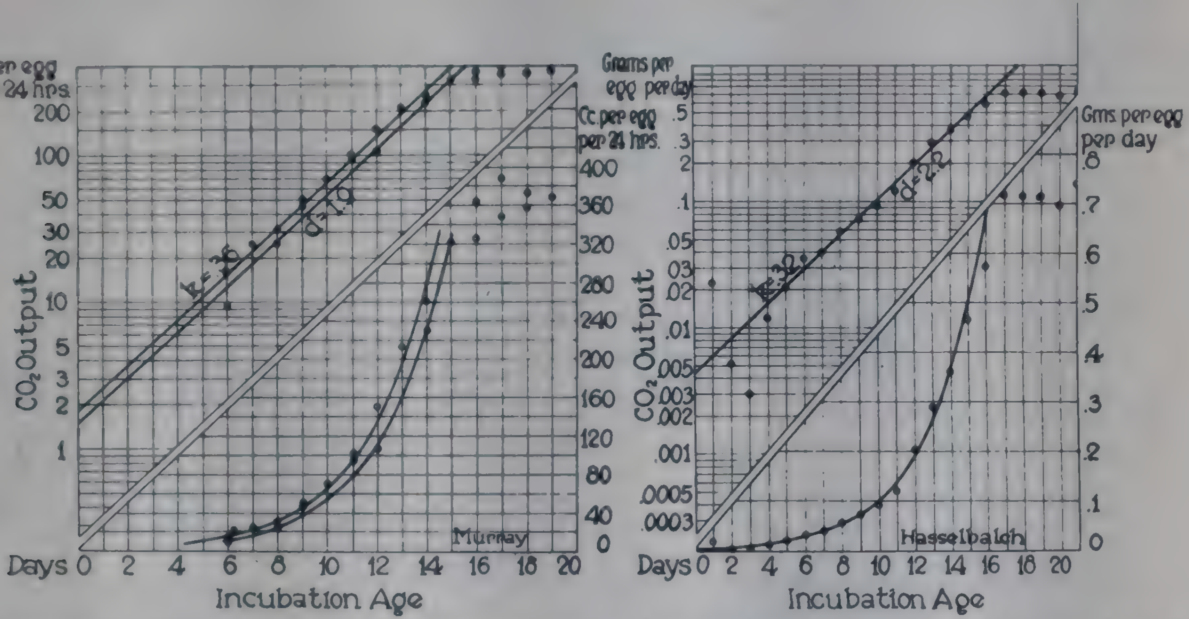

Fig. 16.21. The course of CO_2 excretion in the chick embryo plotted from data by Hasselbalch and by Murray.

It is, of course, impossible to measure the *instantaneous* rate of growth in the laboratory, because of the finite time interval required for making a measurement; but even if it were possible, the experimental errors of measurement would be greater than the instantaneous gains. Here abstract mathematics is used to solve a practical problem. The infinite number of infinitesimal instantaneous rates are added up, or integrated. (The method of integrating is explained in elementary calculus text-books.) The method is outlined symbolically in the following equations.

$$\frac{dW}{dt} = kW \tag{5}$$

$$\int_A^W \frac{dW}{W} = k \int_0^t dt \tag{6}$$

$$\ln W = \ln A + kt \tag{7}$$

$$W = Ae^{kt} \tag{8}$$

In the above equations dW/dt represents instantaneous *absolute* growth rate; $\frac{dW/dt}{W}$ and k represent instantaneous *relative*, or, when multiplied by 100, *percentage* growth rate; e is the base of natural logarithms, $\ln W$ is the natural logarithm of weight W at time t, and A is the natural logarithm of W when $t = 0$.

For purposes of computing the numerical value of the instantaneous relative growth rate, k in equation (8) is written in the form

$$k = \frac{\ln W_2 - \ln W_1}{t_2 - t_1} \tag{8a}$$

That is, the instantaneous relative growth rate, k, is the difference between the *natural* logarithms of weights W_2 and W_1, divided by the time interval $t_2 - t_1$. Thus the practically impossible task of *measuring* the instantaneous growth rate is made possible by a mathematical device.

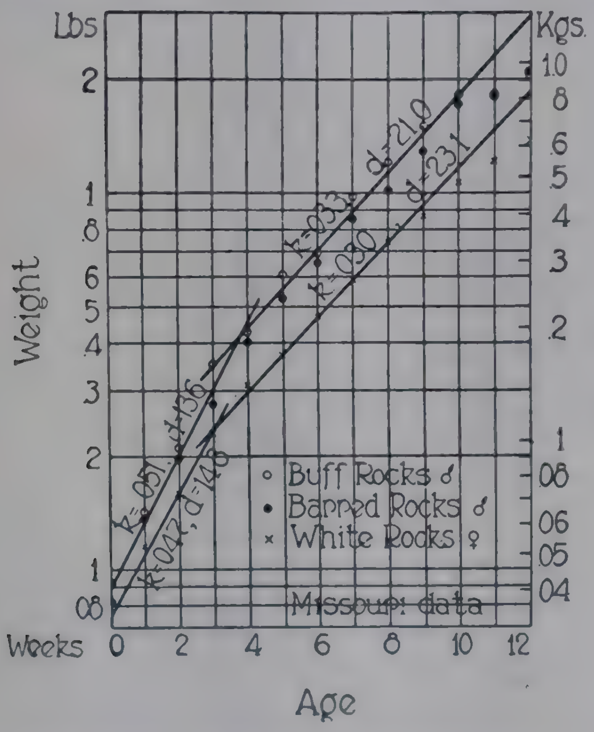

Fig. 16.22. Postnatal growth of the domestic fowl during the self-accelerating phase of growth. During the first month, the growth rate is 5 per cent per day (body doubled in 13.8 days). During the following 7 weeks, the growth rate is 3 per cent per day (body is doubled in 23 days).

The constant k has a perfectly definite meaning. It is the instantaneous relative rate of growth for a given unit of time. Thus, for the growth of the fetus of the albino rat, from 14 days to birth, the value of k is 0.53; this means that the instantaneous percentage rate of growth is about 53 per cent per day or $53 \times 30 = 1590$ per cent per month; or $53 \times 7 = 371$ per cent per week, etc. As regards the constant A in equation (8), theoretically it has the value of W when $t = 0$. For the rat, A was found to be 0.00065 gram. This does not imply that at conception the fertilized egg weighs 0.00065 gram, for the constant was obtained on the basis of data from 14 to 22 days only, and one is not justified in extrapolating this value to conception. While, therefore, A has a definite theoretical meaning, practically no significance should be attached to it. Until data become available which indicate the justification of extrapolating the curve to conception, it need be considered merely as a parameter of the equation.

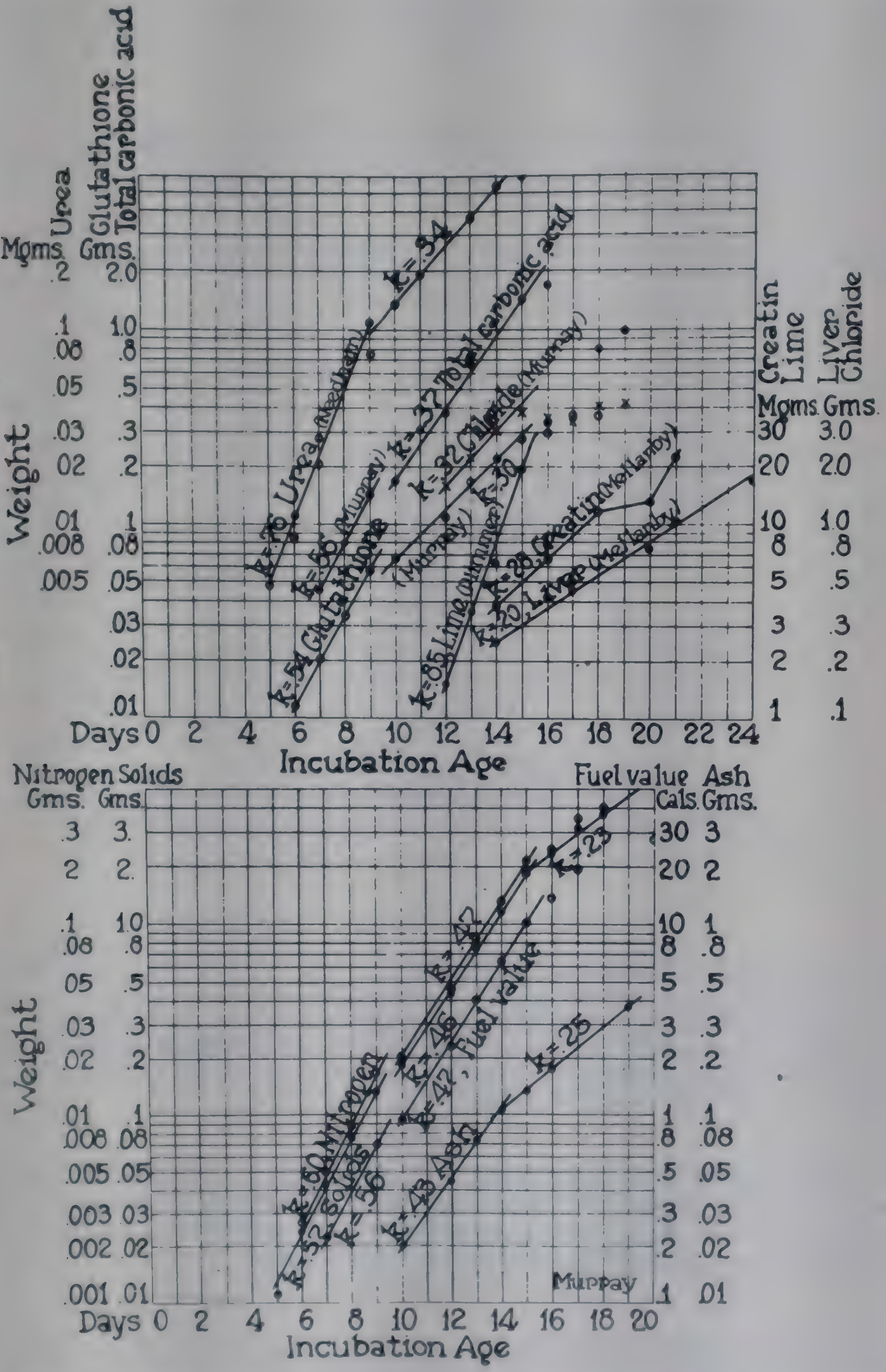

Fig. 16.23a. Prenatal weight growth of the chick embryo and of its constituents and metabolites plotted from several sources on arithlog paper with indicated slopes.

It is instructive to indicate the relation between the instantaneous percentage growth rates as computed by equation (8a) and the conventional percentage growth rate computed by equation (2), which is the method proposed by Minot[21], used almost universally by biologists until the appearance of our 1927 paper[22].

We may take for illustration the data on fetal growth of the albino rat[23], ages 13 to 22 days. According to Minot, the computation for evaluating relative rates of growth is carried on as follows:

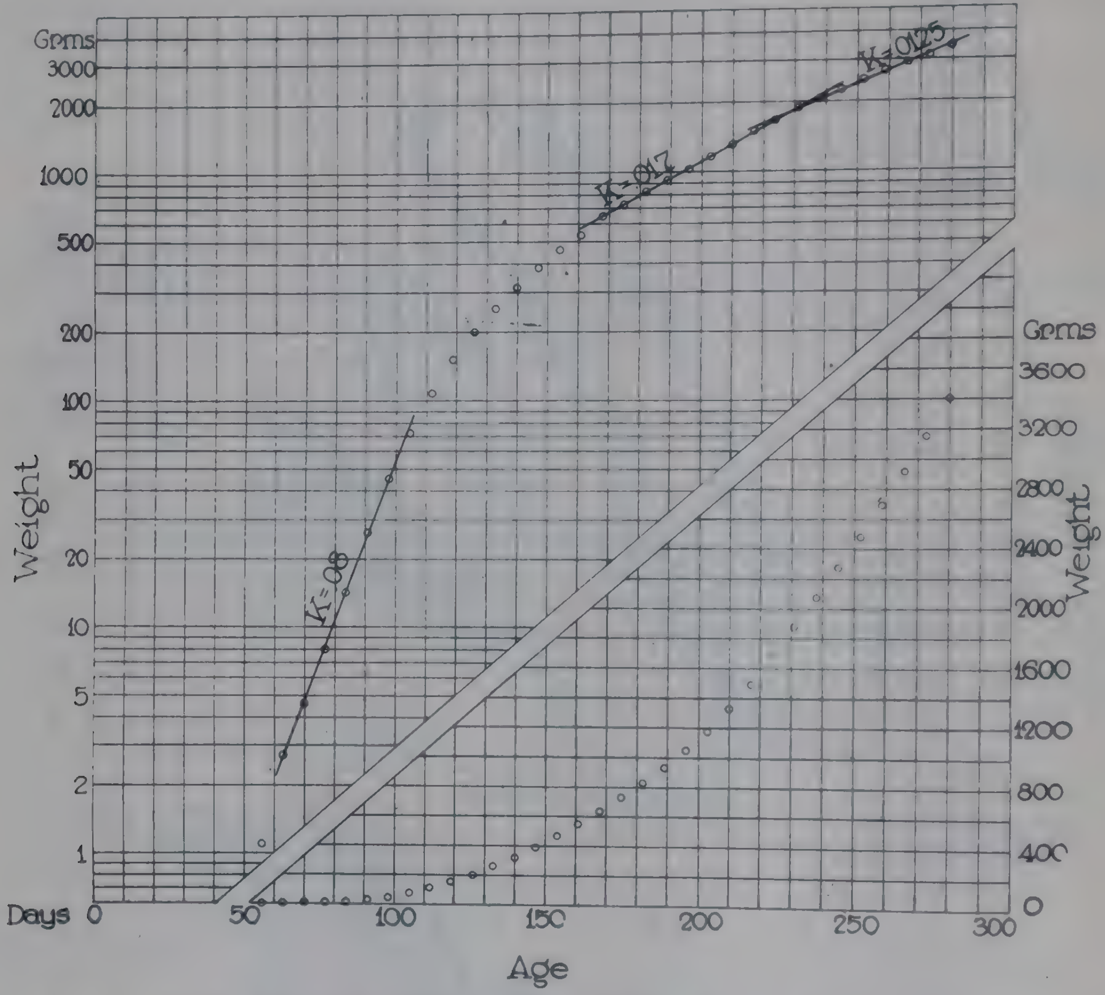

Fig. 16.23b. Prenatal weight growth in man, plotted from Streeter on arithlog paper. During the period 50 to 100 days prenatal life, growth occurs at 8 per cent per day (body weight is doubled once in 8.7 days); between 160 and 230 days, at 1.7 per cent per day (body weight doubled in 41 days); between 240 and 280 days at 1.3 per cent per day (body weight doubled in 55 days). Eight per cent per day is equivalent to 240 per cent per month; 1.7 per cent per day is equivalent to 51 per cent per month; 1.25 per cent per day is equivalent to 37.5 per cent per month.

Take the weight at a given age, and the weight at the next older age for which there are observations. From these data calculate the average daily increase in weight for the period between the two determinations of weight, then express the daily increase in percentage of the weight at the beginning of the period.

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[21] Minot, C. S., "The problem of age growth and death," New York, 1908; also *J. Physiol.*, **12**, 97 (1891).

[22] Univ. Mo. Agr. Exp. Sta. Res. Bull. 97, 1927. See also Schmalhausen, I., *Arch. Entwicklungsmech. Organ.*, **109**, 455 (1927); **110**, 33 (1927); **124**, 82 (1931).

[23] Stotsenburg, J. M., *Anat. Rec.*, **9**, 667 (1915).

We have shown[24] that our *instantaneous* growth rate, k in equation (8), is related to Minot's *finite* growth rate, R in equation (2), by the logarithmic function

$$k = \ln(R + 1)$$

as illustrated by Fig. 16.9. The difference is particularly striking in growth rate beyond about 10 per cent, as illustrated by the following numerical examples.

At age 13 days, $W_1 = .040$ gram and at 22 days $W_2 = 4.630$ grams. The percentage growth rate, according to the method of Minot (eq. 2), is then $\frac{4.630 - .040}{.040 \times 9} \times 100 = 1275$ per cent per day; according to our method, the true or instantaneous percentage rate, k (eq. 8a), is only $\frac{\ln 4.630 - \ln .040}{9} \times 100 = 52$ per cent per day; depending on the method used, the same set of data yields 1275 per cent or 52 per cent growth rate.

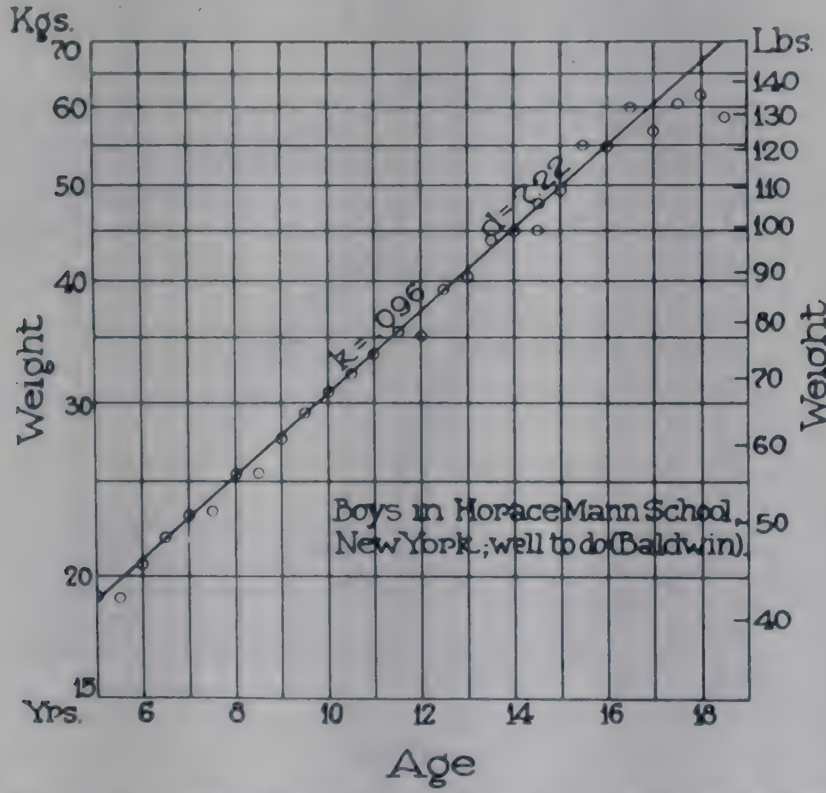

Fig. 16.24. Juvenile growth in man. Well-nourished children grow at an approximately constant percentage rate between 5 and 15 years (about 10 per cent per year; the body weight is doubled once in about 7 years). The prepubertal acceleration, so conspicuous in the literature on growth of children, is usually found only in the curves of poorly nourished children (Figs. 16.50 and 16.52).

The difference in percentage rates as determined by the two methods decrease with decreasing time intervals between weighings. Thus, by reducing the intervals between weighings to 5 days, we have: The fetal weight at 13 days, .040 gram; at 18 days, 1.000 grams; hence $R = \frac{1.000 - .040}{.040 \times 5} \times 100 = 480$ per cent; and $k = \frac{\ln 1.00 - \ln .04}{5} \times 100 =$ 64.4 per cent per day.

Similarly, for a two-day interval (between 13 and 15 days), Minot's arithmetic method yields 90 per cent, whereas our exponential method yields 51.5 per cent per day.

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[24] Univ. Mo. Agr. Exp. Sta. Res. Bull. 97, pp. 18–19, 1927.

If a set of data follows an exponential course (eqs. 7, 8, 9), then, knowing the numerical value of k, it is possible to compute the time required for doubling body weight or population size. The time required for a growing body or population to double itself in size is the ratio of the *natural* logarithm of 2, that is, 0.693 . . . to the value of k. The reason for this is given in the following derivation.

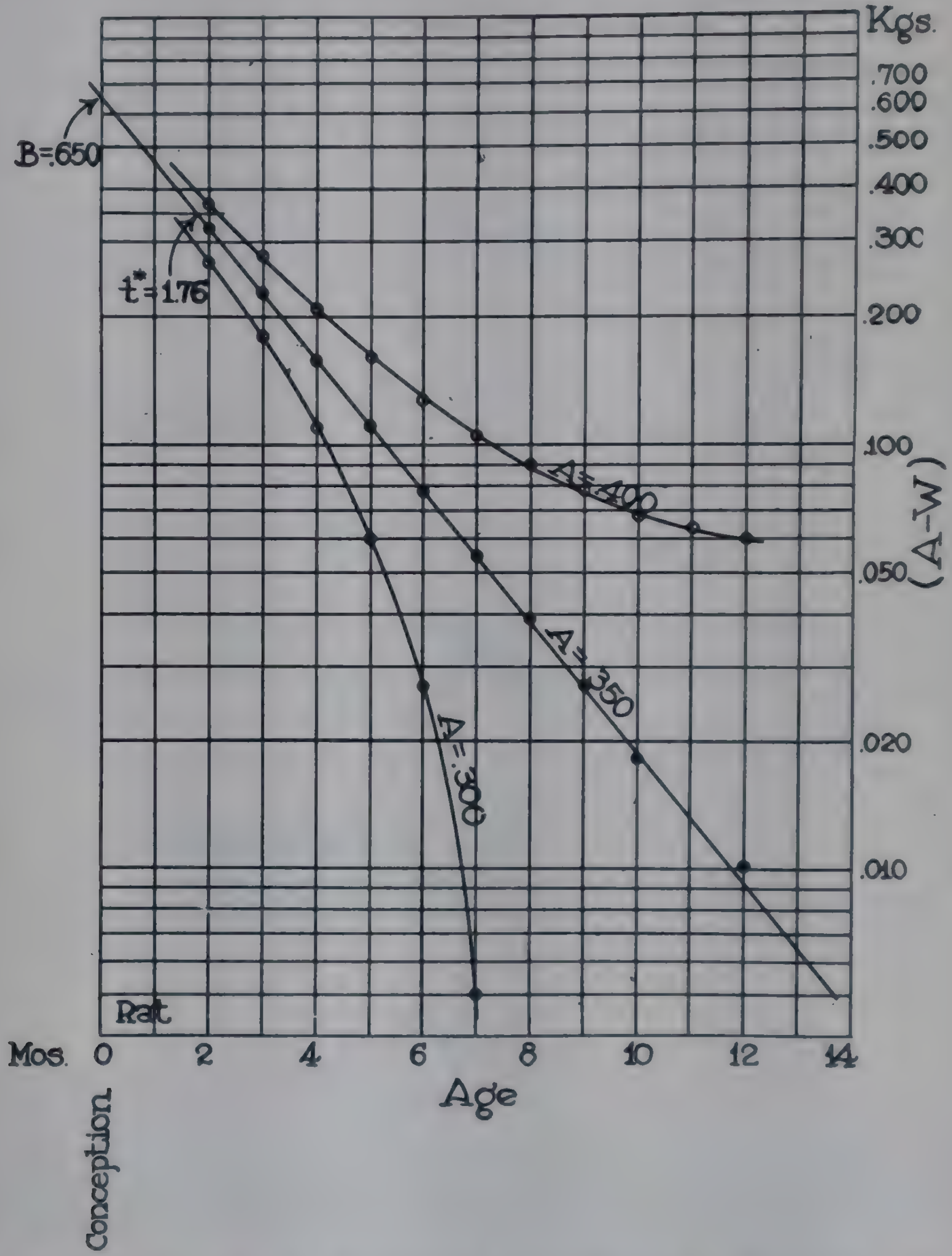


Fig. 16.25. Graphic method for evaluating the constants of equations (12) and (14) for a rat. The correct weight value of the mature weight, A, is 350 gms.; if $(350 - W)$ is plotted against age a straight line results. If a larger or smaller value of A is assumed, the curve deviates from a straight line as indicated. The value of B is read from the curve at the point when $t = 0$; $t^* = 1.76$, the age when $(A - W) = A = 350$ gm.

Solve equation (7)

$$\ln W = \ln A + kt \tag{7}$$

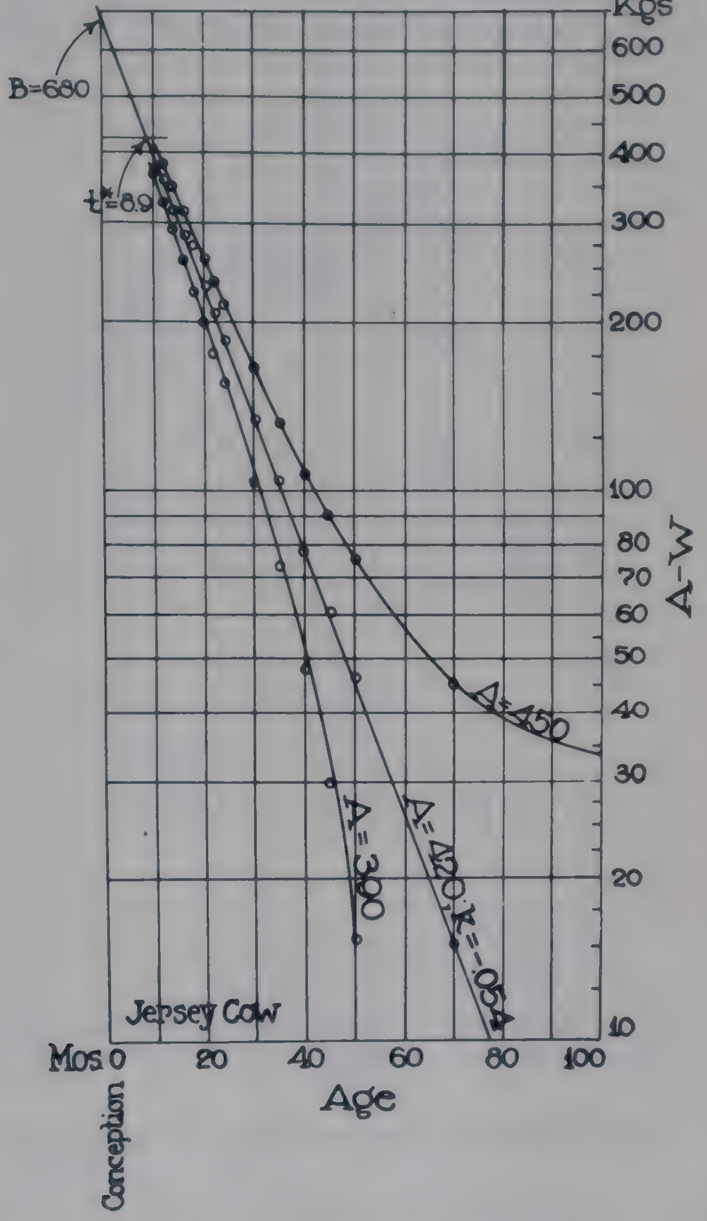
for t,

$$t = \frac{\ln W - \ln A}{k}$$

When the original weight, A, is doubled, W becomes $2A$ and

$$t = \frac{\ln 2A - \ln A}{k} = \frac{1}{k}\ln\frac{2A}{A} = \frac{\ln 2}{k}$$

Fig. 16.26. Graphic method for evaluating the constants for a Jersey cow. A straight line results if A is assumed to be 420 kg, but not 450 or 300 kg; t^* is the age when $A - W = A$, which is 420 kg.



When the percentage growth rate is constant, the time intervals between doubling of weights are constant; therefore, when equation (8) represents growth, the time required for weight to double itself is

$$\frac{\ln 2}{k} = \frac{0.693}{k}$$

Thus, the value of k for fetal growth of the rat was found to be 0.53. Hence, the time required for the rat fetus to double its weight is $\frac{0.693}{0.53} = 1.3$ days; if growth in weight is taken as an index of the increase in the number of cells in the body, then a new generation of cells is produced, on the average, once in 1.3 days; or the cell-division frequency is approximately $\frac{1}{1.3} = 0.77$ per day. It would thus be possible to determine the mean life of a mother cell before it divides into two daughter cells, if increase in weight were a measure of increase in the number of cells in the body.

Let us next apply systematically this method of computing instantaneous percentage growth rates to the analysis of the self-accelerating phase of several other age curves of growth in weight or population size.

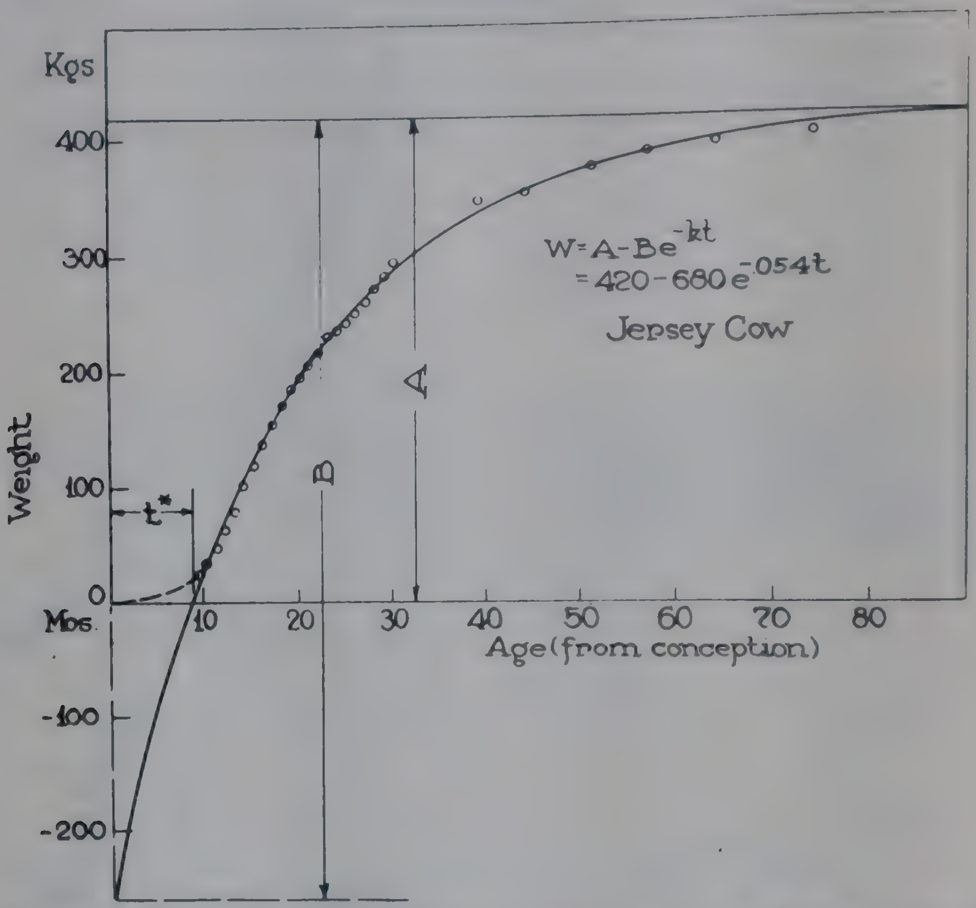


Fig. 16.27. The smooth curve represents equation (12) or (13) for the cow represented in Fig. 16.26. The significance of the constants is indicated graphically.

16.4: The principle of mass action and the self-accelerating phase of growth.

> The first principle in biology is that there is within living substance a condition of internal pressure tending toward expansion of self or kind . . . the tendency to take in and assimilate everything assimilable . . . to grow, to multiply. *R. E. Coker*

As explained in the preceding section, the age curve of growth is sigmoid in form (Fig. 16.5) consisting of a self-accelerating phase of increasing slope and a self-inhibiting phase of decreasing slope. The two are joined during puberty in animals, flowering in plants, and "coming of age" in populations of organisms. Let us rationalize the segment of increasing slope with the aid of the principle of mass action.

According to this principle as it is employed in chemistry, the speed of a chemical reaction is, in the simplest case (reaction of the first order), and when other conditions are equal, proportional to the number of available units (molecules, ions, etc.) entering into the process at the given instance. This principle, then, involves the conception of constancy of percentage rate. It is the principle of compound interest, with the "interest added to the capital continuously from moment to moment", rather than annually, semi-annually, or quarterly as is financially common.

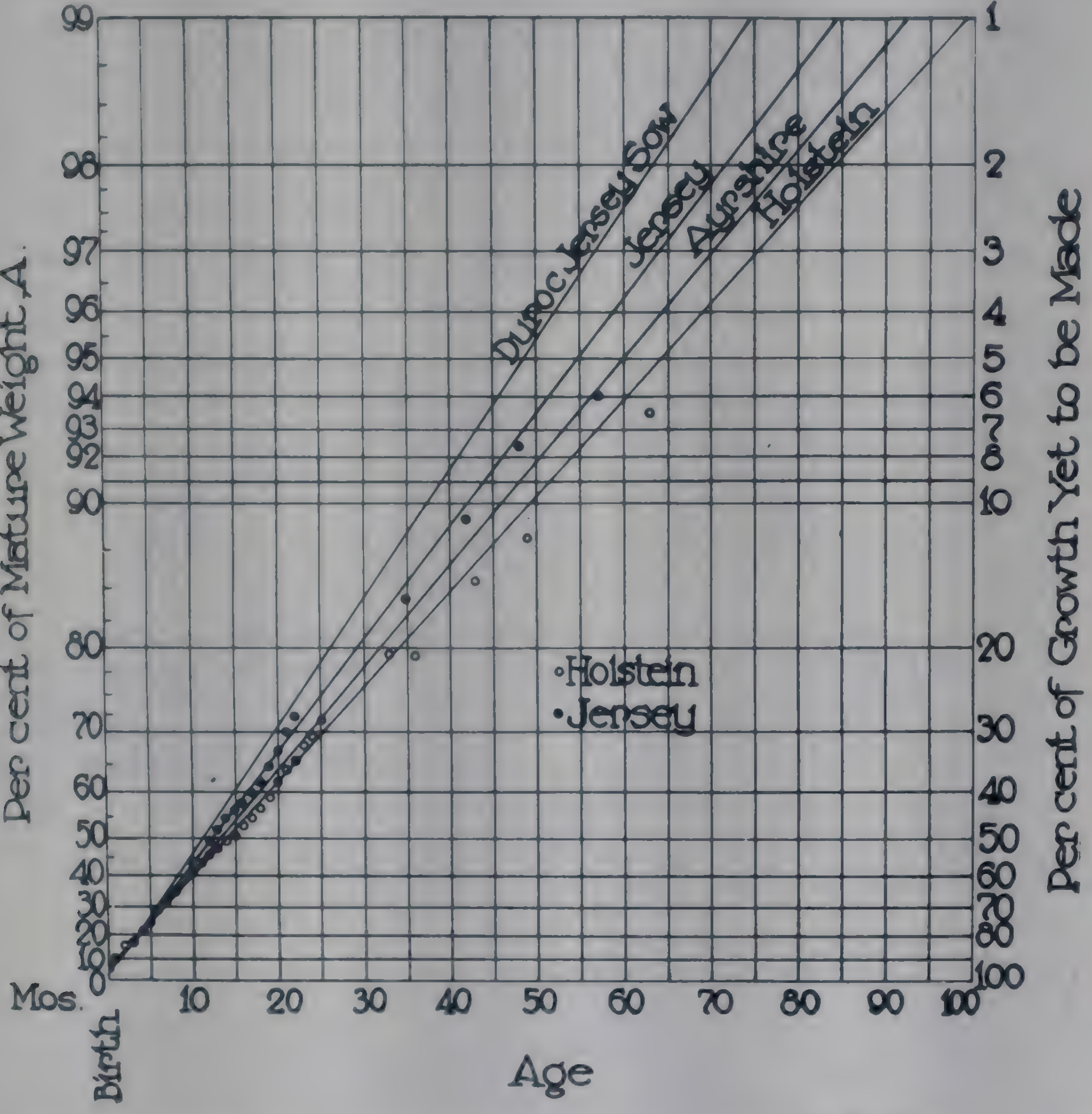


Fig. 16.28. A straight line form of the growth curve. $100\,(l - \frac{W}{A})$ was plotted against age on arithlog paper. The Holsteins attained 80 per cent of their mature weight at 34 months, Jerseys at 28 months.

Equation (5)

$$\frac{dW}{dt} = kW \qquad (5)$$

and its integrated form

$$W = Ae^{kt} \qquad (8)$$

are thus essentially the equations of the physical chemist for the kinetics of monomolecular change. The time curve of early growth, of biosynthesis, is, as might be naturally expected, similar to that of chemical reactions in general. This statement does not at all imply that growth is a "simple monomolecular chemical reaction", or that it is even limited by such a reaction. It merely calls attention to a similarity in general plan, to a general analogy. The principle of mass action is applicable to the multiplication rate of any category of reproducing units whenever the reproduction rate tends to be directly proportional to the number of reproducing units. Thus when other conditions are equally favorable, one bacterium divides into 2, 2 to 4, 4 to 8, and so on in a geometric progression.

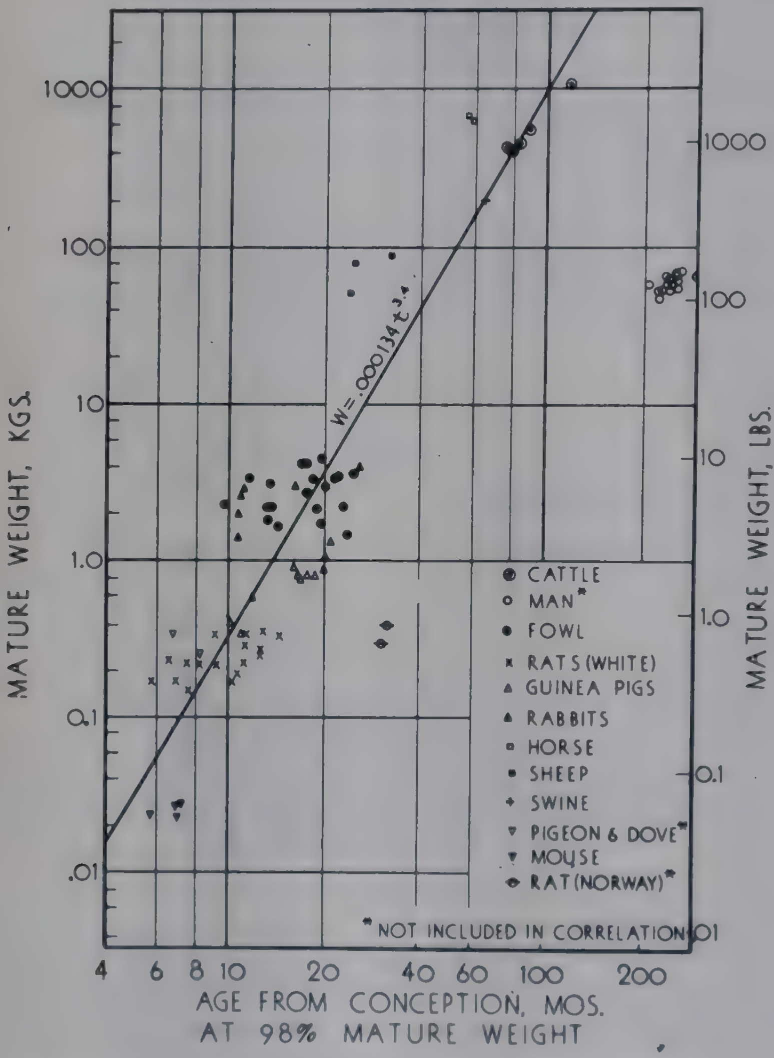


Fig. 16.29. The relation between the mature weight, A, and the speed of approach to the mature weight during the self-retarding phase of growth.

The term k in equation (8) is the velocity constant of the physical chemist, or the (instantaneous) growth *rate* (relative rate, or percentage rate when multiplied by 100) of the biologist.

Equation (8) may be fitted to data by the method of least squares or graphically. In either case, it is first "rectified", *i.e.*, written in linear form, by taking logarithms of both sides:

$$\ln W = \ln A + kt \tag{7}$$

which has the same form as the linear equation $y = a + bx$

$\ln W$ corresponding to y, $\ln A$ to a, and kt to bx.

Therefore, if the logarithms of W (weight) are plotted against the corresponding values of t (age), a straight line results of *slope* k, and intercept nA, and the equation is thus fitted graphically to the data.

Since the eye is sensitive to deviations from a straight line, it is easy to judge whether equation (7) represents the course of change. Whenever the equation fails to represent the data, notice is registered by deviation from the straight line.

Instead of plotting logarithms, the original data may be plotted on arithlog paper, the vertical axis of which is divided logarithmically and the horizontal axis arithmetically. We shall use this method because it saves the labor of looking up logarithms and keeps before us the meaningful original data instead of logarithms, which are vague to most of us.

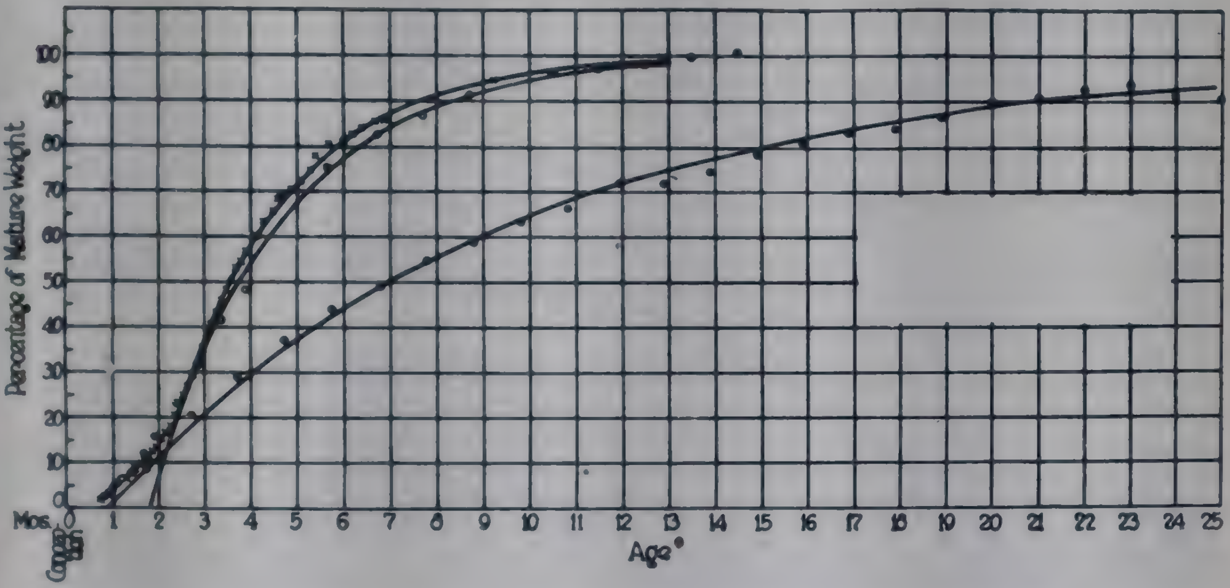


Fig. 16.30. Relative speeds of approach to the mature weight of albino and Norway rats. Both are plotted in terms of the percentage of mature weight. One month in the albino rat is equivalent in speed of approach to mature weight to 3.3 months in the Norway rat. The upper curves represent albino rats respectively of Donaldson and of Greenman; the lower curve represents Norway rats of King.

The fact that the paper is divided on a decimal scale gives the slope, k, of equation (7), a value in terms of common logarithms. This value is converted into natural logarithms by dividing the observed slope by 2.3 ($\ln 10 = 2.302\ldots$).

The equation may be fitted by the method of least squares (appendix to Ch. 13), but only after the data have been plotted on arithlog paper to ascertain that there are no breaks in the curve and that the distribution of the data on the arithlog grid is linear. Equation (7) may be fitted only to data distributed linearly on the arithlog paper.

Fig. 16.10 shows the same (Stotsenburg) rat-growth data on arithlog paper (upper left) and also on arithmetic paper (lower right). The arithmetic curve has an increasing slope. The curve drawn through the arithlog curve has a constant slope, k. Equations (7) or (8) thus represent satisfactorily the course of growth of the rat fetus from 14 days after conception to birth, and the instantaneous growth rate is constant—53 per cent per day as given by the equation fitted to the data

$$W = .000065e^{0.53t}$$

If this reasoning is sound, we have reached the important conclusion that the instantaneous percentage growth rate remains constant during the physiologically enormous period from 14 days after conception to birth.

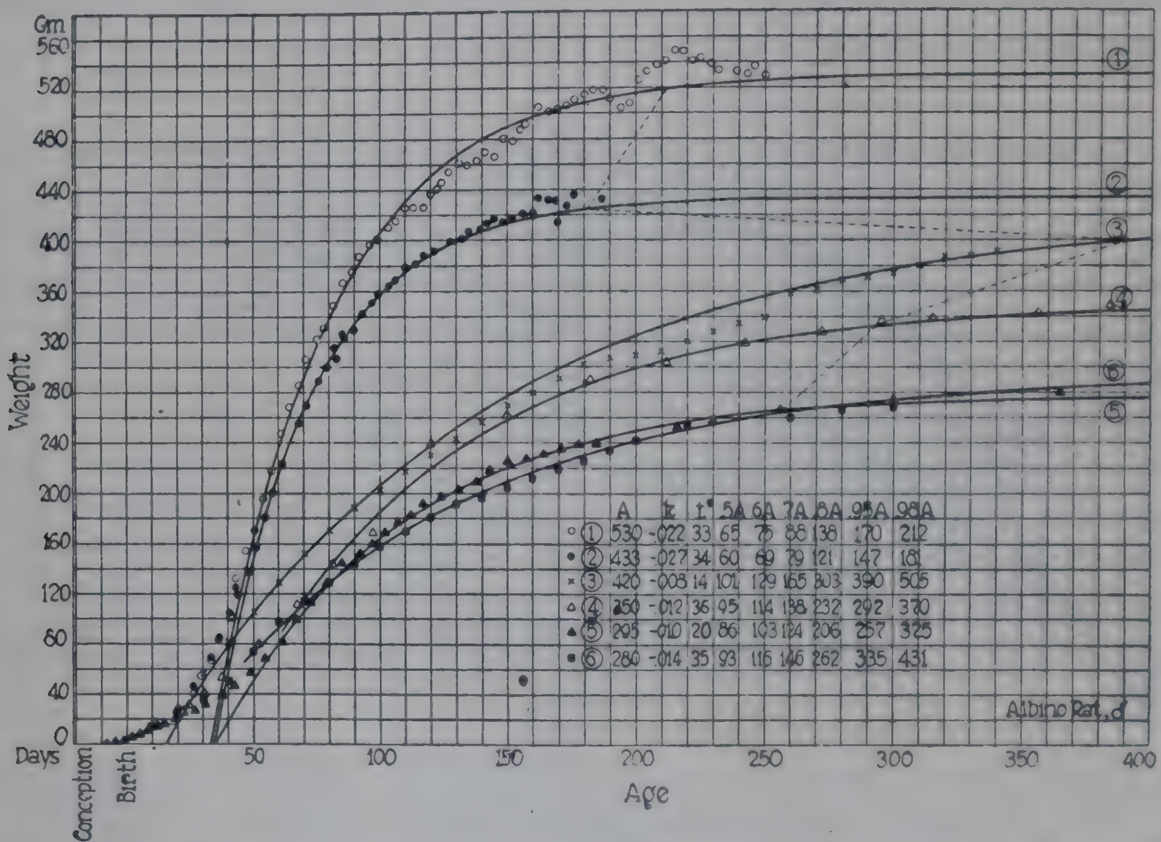


Fig. 16.31. Relative approach to the mature weight of rats on normal diets (numbers 3, 4, 5, and 6) and "maximum-growth" diets (numbers 1 and 2). Curve 1 represents rat 3414 of Osborne and Mendel, curve 2, the average of rats B2135, B2132, B2164, B2161, B3380, B3432, B3414, B3441, B581, B693, B1978, B1974, B2264, B226, B3218 raised on improved diets described in *J. Biol. Chem.*, **69**, 668, (1926). Curve 3 represents Osborne and Mendel's 1925 averages. The points connected by broken curves in Fig. 16.31 represent 98 per cent of mature weight.

The instantaneous percentage growth rate during the 10 days following birth is only about 12 per cent; but it is constant, which is the essential new fact. The constancy of percentage growth rate during the first 10 postnatal days is also indicated in Fig. 16.11, in which the values of $100k$, for 3 sets of rats, are plotted against age; the resulting curves are horizontal, that is, the percentage rate of growth is practically constant. The break in the curve at birth is, among other factors, associated with a radical change in the mode of life.

In Fig. 16.12 the data during the first 10 days following birth are plotted again, together with the remaining data for the phase of growth preceding the inflection. From conception age 32 days (10 days after birth) to 52 days, the instantaneous growth rate appears to be 4 per cent per day; from 52 days up to the inflection (about 85 days after conception, 65 days after birth) 3 per cent per day. (We are not certain of the presence of later breaks.) The breaks are also illustrated in the increment curve[25] of Fig. 16.13. The conclusion is, then, that while the percentage growth rate declines with age, the decline is much slower than has ever been thought before, and the decline does not appear to be continuous. The percentage growth rate remains relatively constant between rather wide limits, and then declines relatively abruptly to a new low level.

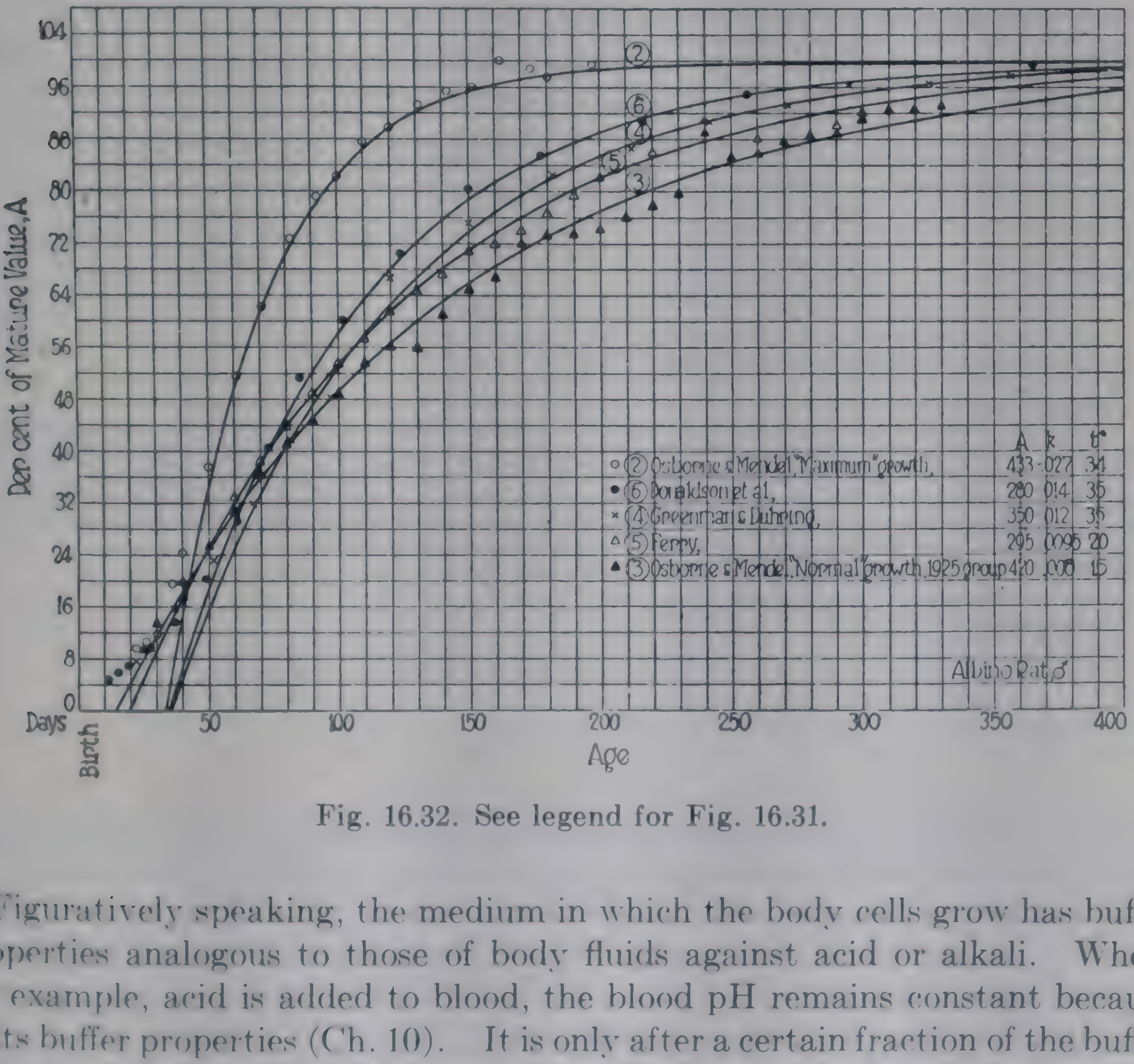


Fig. 16.32. See legend for Fig. 16.31.

Figuratively speaking, the medium in which the body cells grow has buffer properties analogous to those of body fluids against acid or alkali. When, for example, acid is added to blood, the blood pH remains constant because of its buffer properties (Ch. 10). It is only after a certain fraction of the buffer is "spent" that the acidity exceeds a certain threshold, or critical value, and affects the welfare of the organism. May not an analogous situation exist with respect to the growth-retarding substances in the body?

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[25] Weight increments increase at the same percentage rate, $100k$, as the body weight itself.

Indeed, this appears to be the situation for growth of a population of lactic-acid producing organisms in milk, measured by the rate of accumulation of lactic acid in milk, as shown in Fig. 16.14. Neutralizing the lactic acid in the milk is followed by a new cycle of exponential growth (Fig. 18.1).

Fig. 16.15 shows the constancy in the percentage growth rate of *B. coli* (also an acid-producing organism) in broth. This constancy in the percentage growth rate of acid-producing bacteria is due to the high buffer value of the medium, which neutralizes the growth-retarding lactic acid as it is produced, thus keeping the culture in the same state for a relatively long period. When the threshold pH is exceeded, the percentage growth rate declines.

A similar situation prevails in human population growth. When the density of the population is very low during its early history and much more fertile land is available than the population can utilize, the natural increase of the human population occurs at a constant percentage rate. This is illustrated by Figs. 16.16 and 16.56 for the growth of the American Colonies and United States population. This population grew at the instantaneous rate of 2.9 per cent per year from 1660 to 1890. The critical or "threshold value" was reached in 1880, when the growth of the population began to decline (Ch. 25).

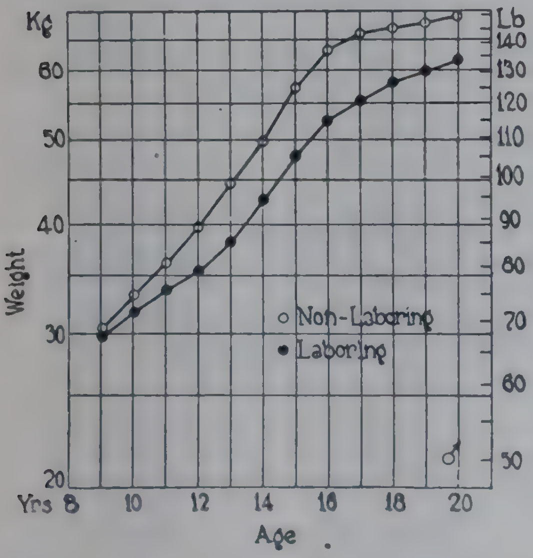

Fig. 16.33. Comparison of growth of English children, "laboring" and "non-laboring." Data by Roberts, compiled by B. T. Baldwin, *Univ. Iowa Studies in Child Welfare*, **1**, 1 (1921).

Fig. 16.17 represents the percentage growth rate (100k) of the rat as a function of age; it indicates the manner of decline in the "growth potential" with increasing age. The graph reminds one of a series of water pipes, each of which is relatively horizontal, has a relatively constant head pressure, and is below its predecessor, finally fading to zero. This is the essential history of a running stream to its ultimate end, and of growth to its ultimate end.

The most striking age curve obtained in this analysis of early growth is shown in Fig. 16.18a, which relates CO_2 production with age in the chick embryo. The age increase in CO_2 production is perhaps a better index of growth than the age increase of weight, since weight increase may be due to increase in relatively inert, or even non-living, matter whereas CO_2 production represents definitely living, metabolizing tissue.

We prepared Fig. 16.18a from data by Atwood and Weakley.[26] Each egg was incubated individually in a glass tube. The data points represent the average daily CO_2 output of the 63 eggs which hatched normal chicks. The circles represent observed values. The relatively high CO_2 output during the first day in comparison to the second is apparent only because the eggs were kept, as is customary, in a cool cellar before incubation. When, therefore, the eggs were subjected to the relatively high incubator temperature, there was in addition to the metabolic CO_2 output an expulsion of the excess CO_2 because of its lower solubility at the incubator temperature. This explanation is substantiated by the data for the CO_2 excretion of a control, infertile, egg represented in Fig. 16.18a by crosses. The CO_2 production during the first day is virtually the same for the control and incubating egg. The CO_2 production associated with incubation is properly represented by the difference between the fertile and infertile control.

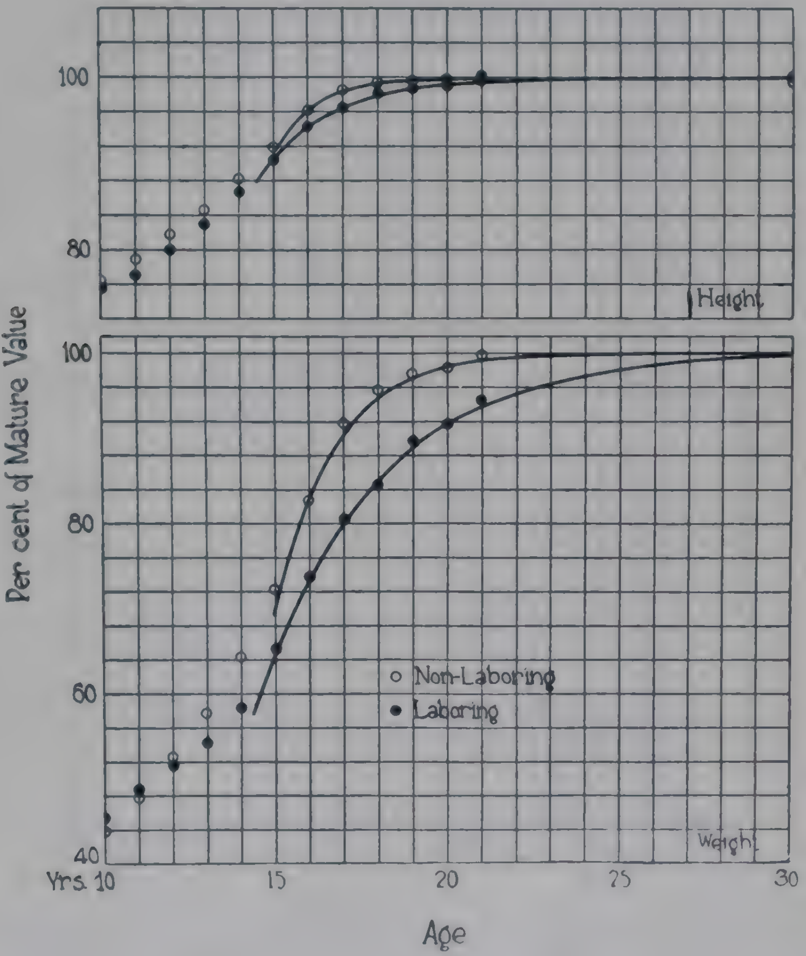

Fig. 16.34. The data in Fig. 16.33 in terms of percentage of mature weight, including data on growth in height.

The distribution of this difference between the CO_2 production of fertile and infertile eggs is fairly linear on the arithlog grid: the instantaneous increase in CO_2 production *during the first four days of incubation* is seen to be of the order of 100 per cent per day. It is interesting to note that the cleavage rate of the rabbit and rat eggs during the first three days of incubation (Fig. 16.2) is of the order of 120 (rat) to 140 per cent (rabbit) per day.

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[26] Atwood, H., and Weakley, C. E., W. Virginia Agr. Exp. Sta. Bull. 185, 1924.

Fig. 16.19 illustrates in a more striking manner the drop in CO_2 production during the second day. Here the percentage increases, $100\ (\ln W_2 - \ln W_1)$, were plotted against age. The greater drop in Bohr and Hasselbalch's curve is probably due to a lower preincubation temperature than in Atwood and Weakley's.

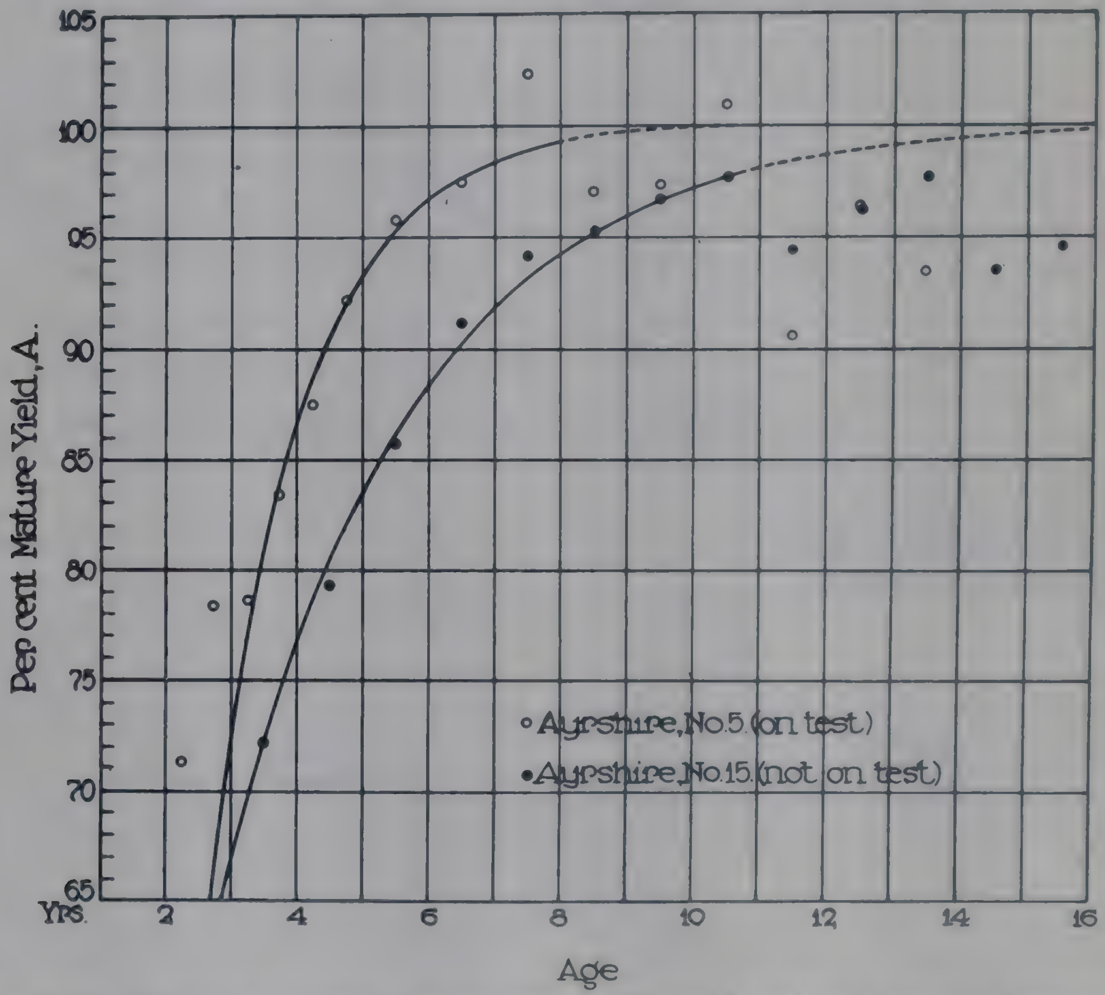

Fig. 16.35. Relative approach to maximum milk yield under Advanced-Registry test and ordinary conditions of management. The better-fed test animals approach the mature level at a more rapid rate.

Returning to Fig. 16.18a, from 4 to 15 days the data points are distributed in a remarkably uniform manner around a straight line, indicating an instantaneous increase of 31 per cent per day. The second remarkable feature of this graph is the pause between 16 and 19 days. The chick no doubt passes a critical period, a "metamorphosis", at this stage. This statement relating to a critical period is substantiated by the mortality curve, Fig. 16.20, which passes a peak at this time. The trigger mechanism in the break may be a change in the mode of respiration: the respiratory function is transferred from the chorioallantoic membrane to the lungs; the chick "metamorphoses" from an aquatic to a terrestrial mode of respiration.

The smaller peak in the mortality curve at about five days may perhaps be correlated with the peak in the lactic-acid curve shown in Fig. 16.20. The mechanism of lactic-acid oxidation apparently does not begin to function efficiently until this time.

Fig. 16.21 represents data of Hasselbalch and of Murray. The distribution of the data points is less regular because of the smaller number of embryos.

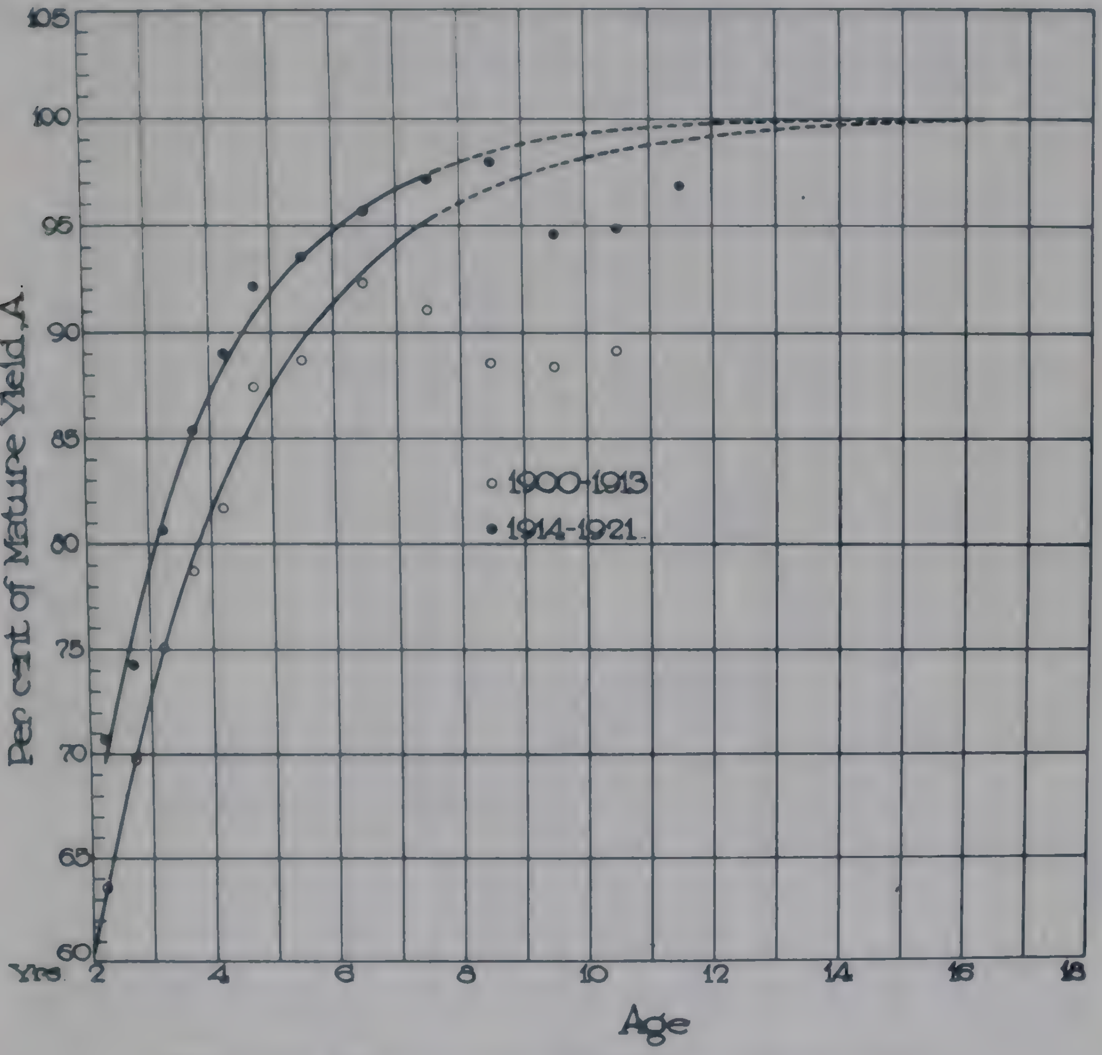

Fig. 16.36. Relative lactation slopes for Jersey cattle.

These charts do not show the last stages of growth; otherwise, the general features of the charts are the same. The values of k for the data of Hasselbalch are the same as those for the data of Atwood and Weakley. The value of k for Murray's data is higher, but this is probably due to a higher incubation temperature. Fig. 16.18b, which represents the age curve of nitrogen storage in the silkworm embryo, is remarkably similar in respect to the growth pause to the age curve of CO_2 excretion in Figs. 16.18a and 16.21.

Fig. 16.22 represents the growth of the fowl during 12 weeks of postnatal life. There appears to be a break in the curve at 3 weeks. The major inflection occurs at the age of about 12 weeks. The values of k during this period are of the same order as those found for the rat.

Humans have a very slow prenatal growth rate in contrast to other species. While the instantaneous prenatal growth rate in the rat is about 53 per cent per day (Fig. 16.10), that of man[27] ranges from a maximum of 8 per cent to a minimum of 1.3 per cent per day (Fig. 16.23b). Therefore, given percentage rates of growth do not indicate equivalent developmental stages. It was already noted (Fig. 16.7) that the age curve of man is distinguished from those of other species by a very long juvenile period. Fig. 16.24 shows that growth during the juvenile period is about 10 per cent per year, that is, only 0.83 per cent (10/12) per month or 0.03 per cent (0.83/30) per day.

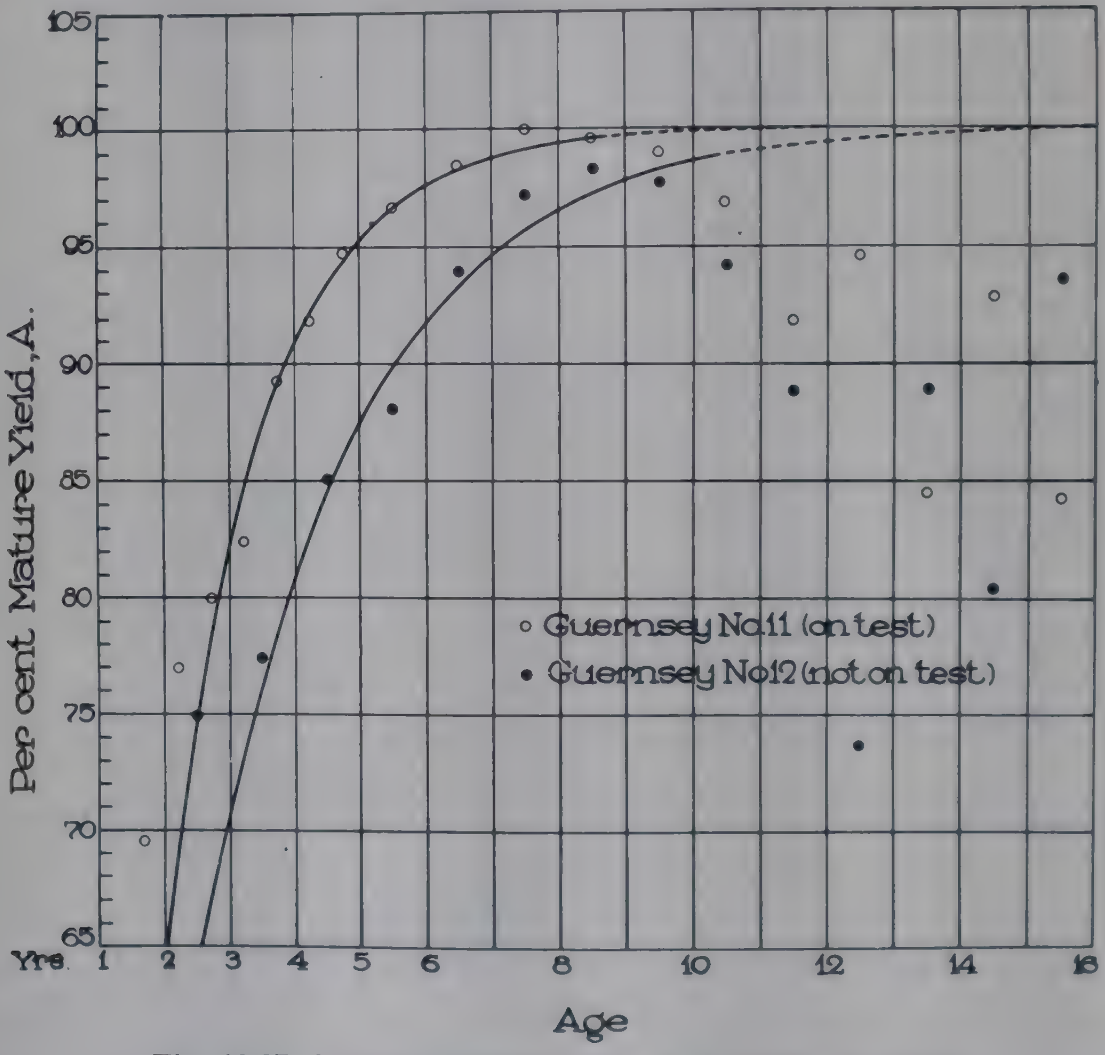

Fig. 16.37. Relative lactation slopes of Guernsey cattle.

16.5: Extension of the principle of mass action to the self-inhibiting phase of growth

> The same path leads up the hill and down. *Heraclitus*
>
> I rise again, changed but the same. *Jacques Bernoulli*
>
> The great object in life of an oyster is to convert the whole world into oysters. The biotic potential of the oyster is limited more by the outside forces than by its own lack of biotic ambition. *R. E. Coker*

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[27] Streeter, G. L., Carnegie Institution of Washington, Contributions to *Embryology*, **11,** 143 (1920).

As previously explained, the age curve of growth may be divided into a self-accelerating phase of increasing slope and a self-inhibiting phase of decreasing slope. During the self-accelerating or unrestricted phase, the time rate of growth tends to be proportional to the size of the individual or of the reproducing population. However, this geometric increase cannot go on indefinitely because of the restricting limitation of the universe. Each lives under a condition not only of pressure from within, tending toward expansion of self or kind to multiply and fill every occupiable niche, but also under a pressure from without which keeps expansive pressure under control.[28]

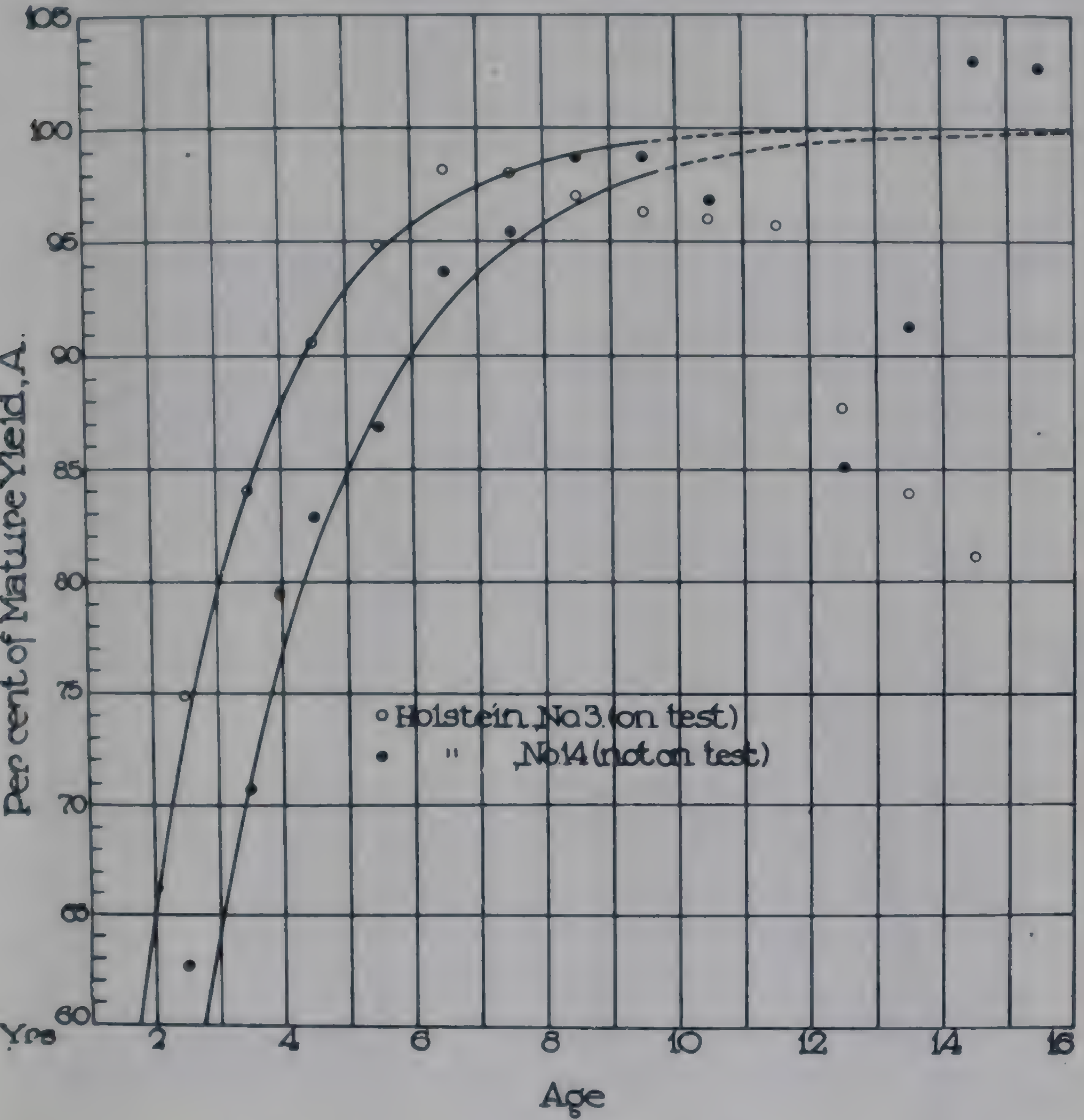

Fig. 16.38. Relative lactation curves of Holstein cattle.

Mention was made of the restrictive effect of the population increase of *Drosophila*, yeast bacteria, on further increase of the population. Analogous restrictive effects may contribute to decline in growth rate of multicellular animals in later growth stages. For instance, the decrease of the ratio of surface to body weight during growth[29] results in progressive congestion in the transportation of nutrients and wastes. One may also mention progressive interference with the transportation of nutrients and wastes through progressive accumulation of inert materials in the body and progressive dehydration and decline in permeability.

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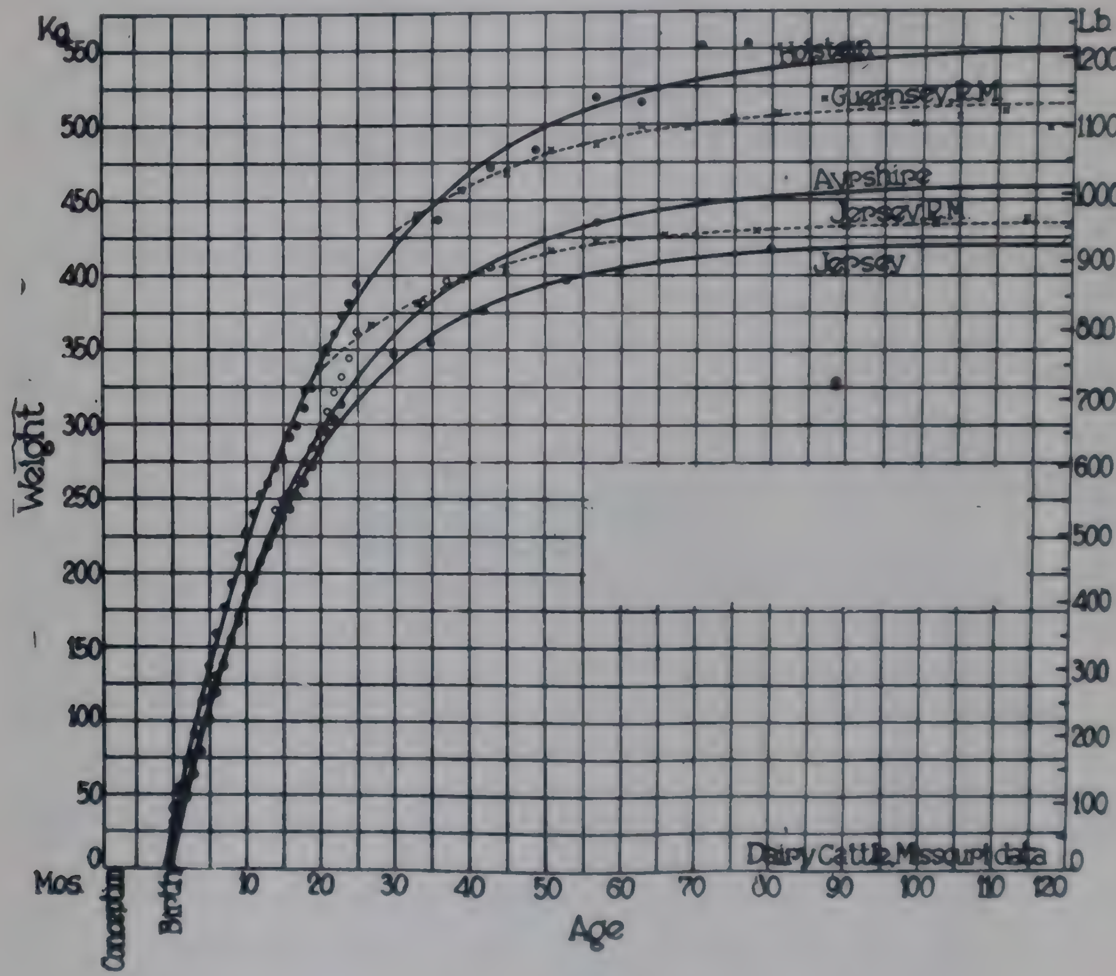
[28] Coker, R. E., *Scientific Monthly*, **48**, 61, 121 (1939).

The mass law equation for the self-inhibiting phase of growth may be formulated just as for the self-accelerating phase, with this difference: during the self-accelerating phase, the growth rate, dW/dt, is proportional to the size of the population or to that of the multicellular individual; during the self-inhibiting phase it is proportional to available "living space", available land, available food supply, available freedom from the deleterious products of growth, and so on. These ideas may be formulated in the conventional terms of the physical chemist, with the symbols used for the self-accelerating phase of growth.



Holstein $A = 550;\ k = -.046;\ t^* = 8.3$
Guernsey, RM $A = 515;\ k = -.044;\ t^* = 0.2$
Ayrshire $A = 460;\ k = -.050;\ t^* = 9.1$
Jersey, RM $A = 436;\ k = -.050;\ t^* = 0.2$
Jersey $A = 420;\ k = -.054;\ t^* = 8.9$

Fig. 16.39. Growth of dairy cattle.

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[29] Cohn, A. E., and Murray, H. A., Jr., *Quart. Rev. Biol.*, **2**, 469 (1927).

Let A represent the limiting food required to attain maximum individual r population size, and W the food supply at the given time; $(A - W)$ then epresents the concentration of the limiting food supply at the moment just ufficient to permit attainment of maximum individual or population size.

It is reasonable to assume that the instantaneous growth velocity, dW/dt, at the given time will be proportional to the concentration of the limiting food supply, that is, to the value $(A - W)$

$$\frac{dW}{dt} = -k(A - W) \tag{9}$$

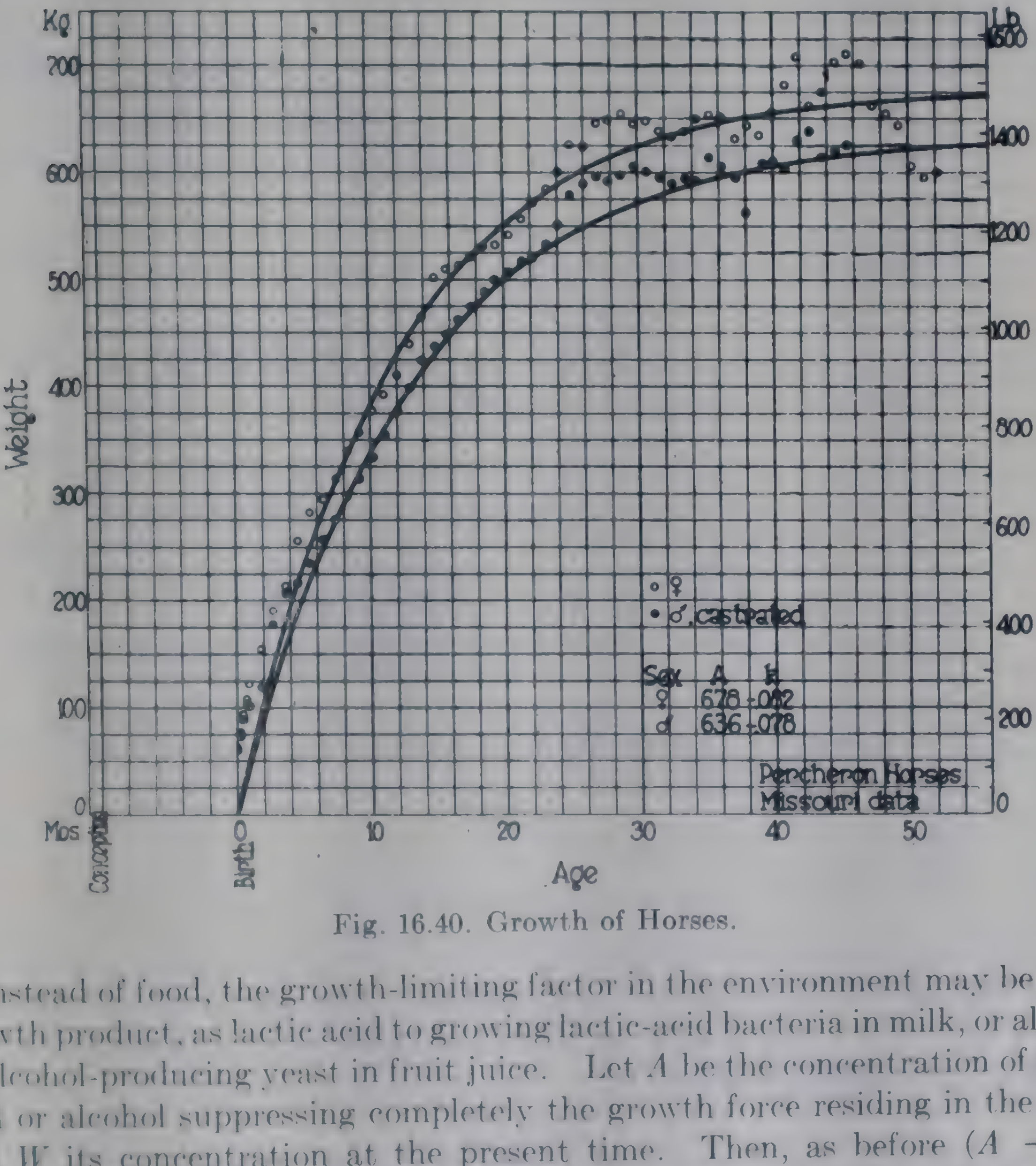


Fig. 16.40. Growth of Horses.

Instead of food, the growth-limiting factor in the environment may be some growth product, as lactic acid to growing lactic-acid bacteria in milk, or alcohol to alcohol-producing yeast in fruit juice. Let A be the concentration of lactic acid or alcohol suppressing completely the growth force residing in the cells, and W its concentration at the present time. Then, as before $(A - W)$ represents the amount of growth which the environment will permit in order to bring the population to the maximum size, A, and $\frac{dW}{dt} = -k\,(A - W)$, the instantaneous velocity of growth at the given time. Analogous reasoning applies to the growth of multicellular animals, which are cell populations, after all.

The numerical values of the constants are estimated as follows: A, which represents the concentration of the growth-limiting factor when growth is completely inhibited, may be used to represent the mature weight of the animal (or the maximum size of the population) under a given set of conditions; W may be used to represent the weight of the animal (or size of the population) at the given time; $(A - W)$ then represents the amount of growth yet to be made to reach the mature weight.

Although equation (9) appears to differ from equation (5), both represent the mass law (for a first-order process); both represent a direct proportionality between growth velocity, dW/dt, and some growth-limiting factor. In equation (5) the growth-limiting factor is W, the growth already made; in equation (9) it is $(A - W)$. In equation (5), k is the relative growth rate with respect to the growth already made,

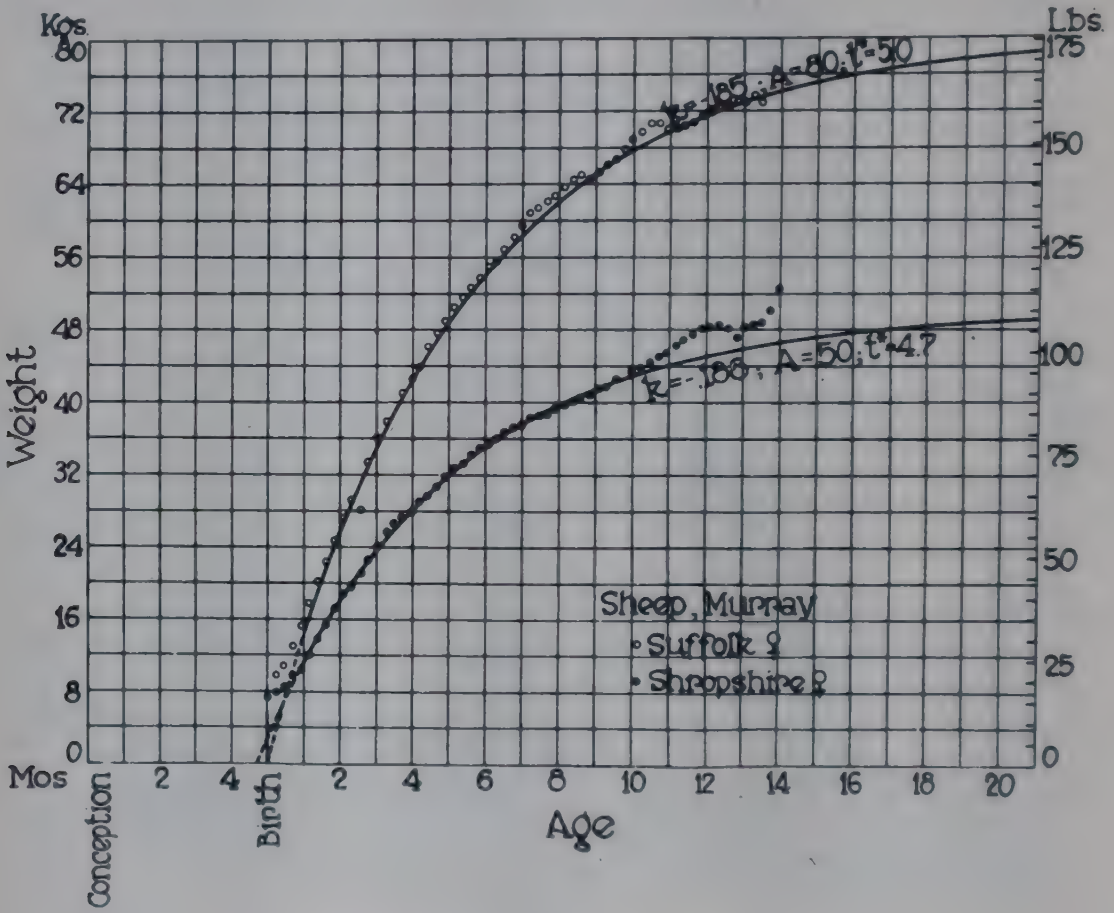


Fig. 16.41. Growth of Sheep.

$$k = \frac{dW/dt}{W} \tag{5}$$

while in equation (9) k is the relative growth rate with respect to the growth yet to be made

$$-k = \frac{dW/dt}{A - W} \tag{9}$$

Before applying equation (9) to data, it is integrated, for reasons explained n the preceding section:

$$dW/dt = -k(A - W) \tag{9}$$

$$\frac{dW}{A - W} = -kdt$$

$$\ln (A - W) = -kt + \ln B \text{ (integration constant)} \tag{10}$$

$$A - W = Be^{-kt} \tag{11}$$

$$W = A - Be^{-kt} \tag{12}$$

The significance of the constancy of the exponent k is that the growth velocity declines at a constant percentage rate $100k$, illustrated by the following numerical example.

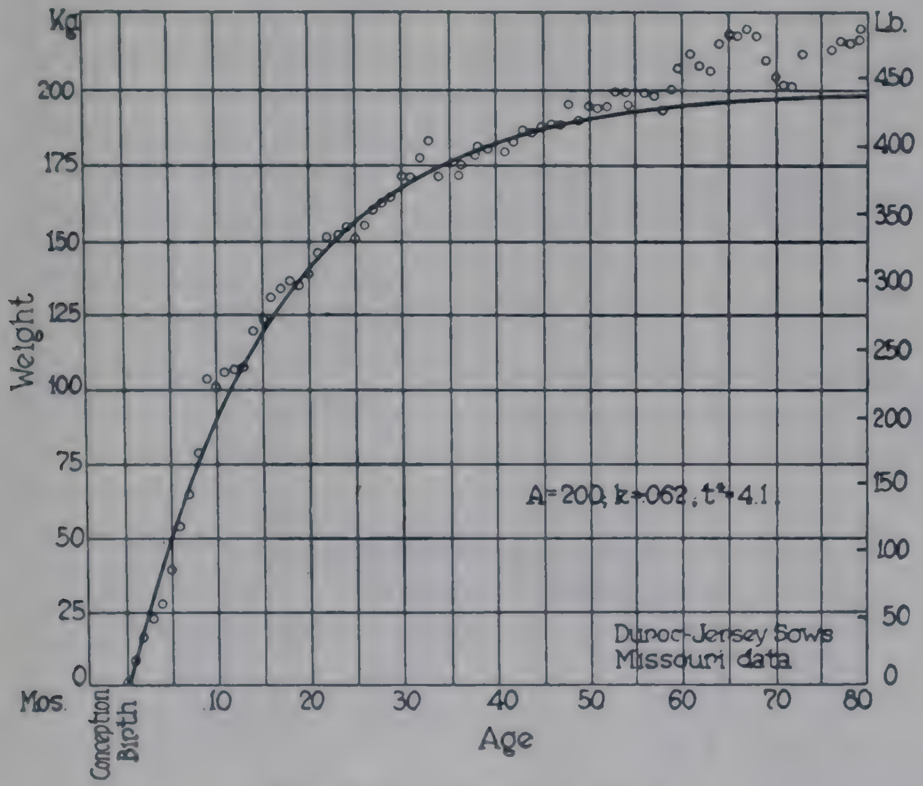


Fig. 16.42. Growth of Swine.

The average increase in weight of guinea pigs in successive months during the self-inhibiting phase of growth was observed to be

112, 90, 70, 56, 45, 35, 27, 21···gms.

The instantaneous relative decline in growth rate was, therefore, in round numbers,

$$\frac{112 - 90}{112} = \frac{90 - 70}{90} = \frac{70 - 56}{70} = \frac{56 - 43}{56} = 0.22, \text{ or 22 per cent per month.}$$

Just as $100k$ represents the percentage *decline* in growth, so $100p$ represents the percentage *persistency* of growth. Thus in the above example for guinea pigs which gained in successive months

112, 90, 70, 56, 45, 35, 27, 21···gms.

the *persistency* of growth is

$$\frac{90}{112} = \frac{70}{90} = \frac{56}{70} = \frac{43}{56} = \frac{35}{43} = \frac{27}{35} = \frac{21}{27} = \cdots = 0.78 \text{ or } 78 \text{ per cent per month.}$$

It is obvious that the sum of the percentage decline and percentage persistency of growth must equal to 100 per cent

$$78 \text{ per cent} + 22 \text{ per cent} = 100 \text{ per cent}$$

The minus sign of k in equation (9) indicates a decline in growth velocity.

The fit of equation (12) to growth data may, as before, be ascertained by the graphic method. The logarithmic form (equation 10) is used for this purpose. $(A - W)$ is plotted against age, t, on arithlog paper. A straight line results if the proper value of A is chosen, and if the equation represents the data. Several values of A are chosen, and $A - W$ plotted. There is an upward curvature for high values of A, a downward curvature for low values of A, and linear distribution for the correct value of A.

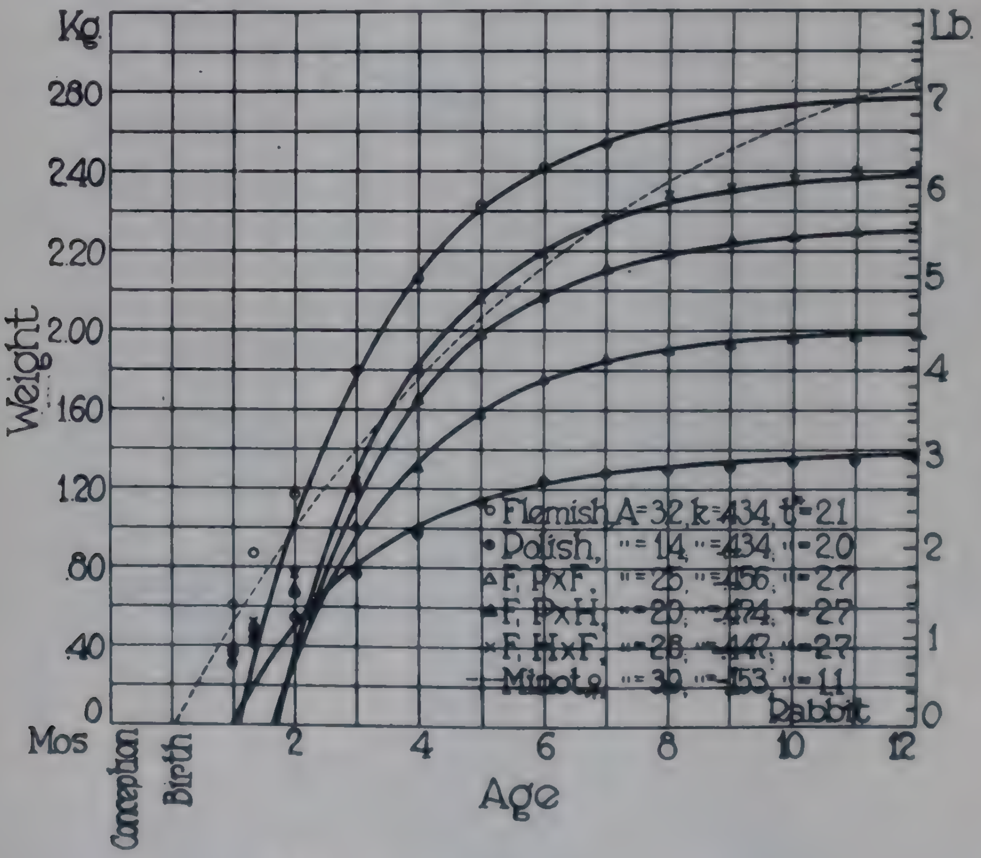


Fig. 16.43. Growth of Rabbits (Castle).

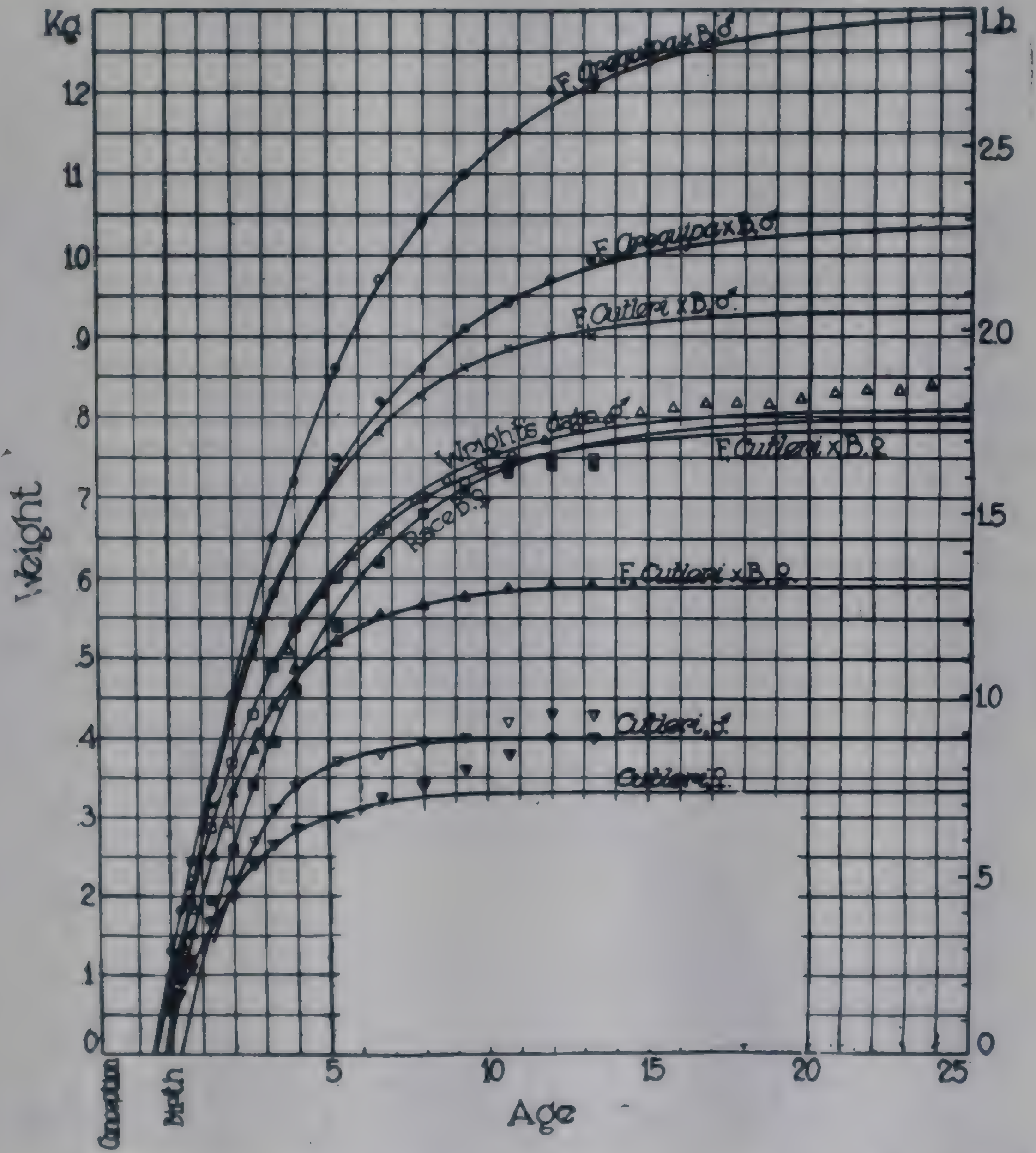
This method of fitting the equation is illustrated in Figs. 16.25 and 16.26. The data points seem to be distributed around a straight line in a satisfactory manner if a correct value of A is chosen. Growth curves drawn according to equations (12) and (14) corresponding to Fig. 16.26, are shown in Fig. 16.27. The agreement between observed and computed values appears satisfactory (of course this applies only to the phase of growth following the inflection).

The value of k is determined by measuring the slope on the arithlog paper (Figs. 16.25 and 16.26) as was done for the self-accelerating phase of growth. B is the intercept of the curve on the arithlog chart; that is, the value of $(A - W)$ when $t = 0$. B may, of ourse, be evaluated algebraically

$$A - W = Be^{-kt} \tag{11}$$

$$\therefore B = \frac{A - W}{e^{-kt}} = (A - W)e^{kt}$$

The constant B may be dispensed with. It is merely an age-parameter (integration onstant) employed to correct for the fact that while age is counted from birth or con-



F, Arequipa × Race B, ♂, $A = 1.300$, $k = -.198$, $t^* = 2.05$
F, Arequipa × Race B, ♂, $A = 1.040$, $k = -.209$, $t^* = 1.63$
F, Cutleri × Race B, ♂, $A = .930$, $k = -.274$, $t^* = 2.00$
Wright's data, ♂, $A = .810$, $k = -.249$, $t^* = 2.10$
Race B, ♀, $A = .800$, $k = -.247$, $t^* = 2.60$
F, Cutleri × Race B, ♀, $A = .785$, $k = -.261$, $t^* = 1.80$
F, Cutleri × Race B, ♀, $A = .590$, $k = -.405$, $t^* = 2.22$
Cutleri, ♂, $A = .400$, $k = -.529$, $t^* = 2.74$
Cutleri, ♀, $A = .333$, $k = -.434$, $t^* = 1.95$

Fig. 16.44. Growth of guinea pigs (Castle).

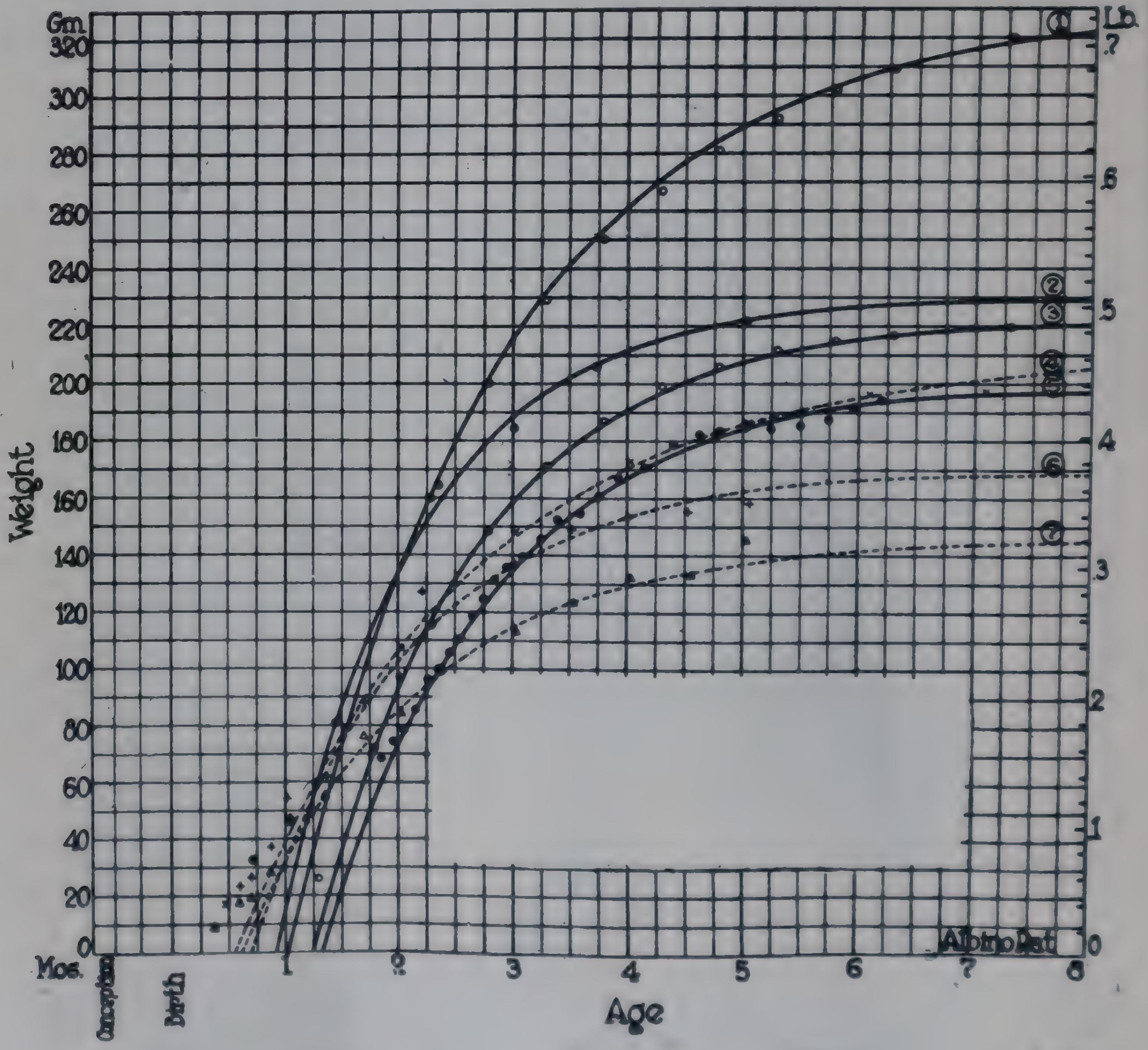
ception, equation (12) fits the data only during the phase of growth following the inflection. This correction may be made in the exponent. The $(A - W)$ curve on the arith-log paper (Figs. 16.25 and 16.26) is extrapolated and the value is read at the point where $(A - W) = A$, that is, when $W = 0$. This is the position at which the extrapolated curve of equation (12) meets the age-axis. By beginning to count age from this point designated by t^*, equation (12) is changed to

$$W = A - Ae^{-k(t-t^*)} \tag{13}$$

since when $t = t^*$, $A = B$.

Equation (13) may be made more elegant by writing it in the form

$$\frac{W}{A} = 1 - e^{-k(t-t^*)} \tag{14}$$



	k	A	t^*	Sex	Notes	Source
1.	−.520	330	1.71	♂		Sherman
2.	−.810	230	1.62	♂		Hoskins
3.	−.707	223	1.95	♀		Sherman
4.	−.485	210	1.25	♀		King
5.	−.644	203	2.03	♀		Donaldson
6.	−.707	170	1.40	♀	Litter mate to runt	King
7.	−.621	147	1.30	♀	Runt	King

Fig. 16.45. Growth of rats.

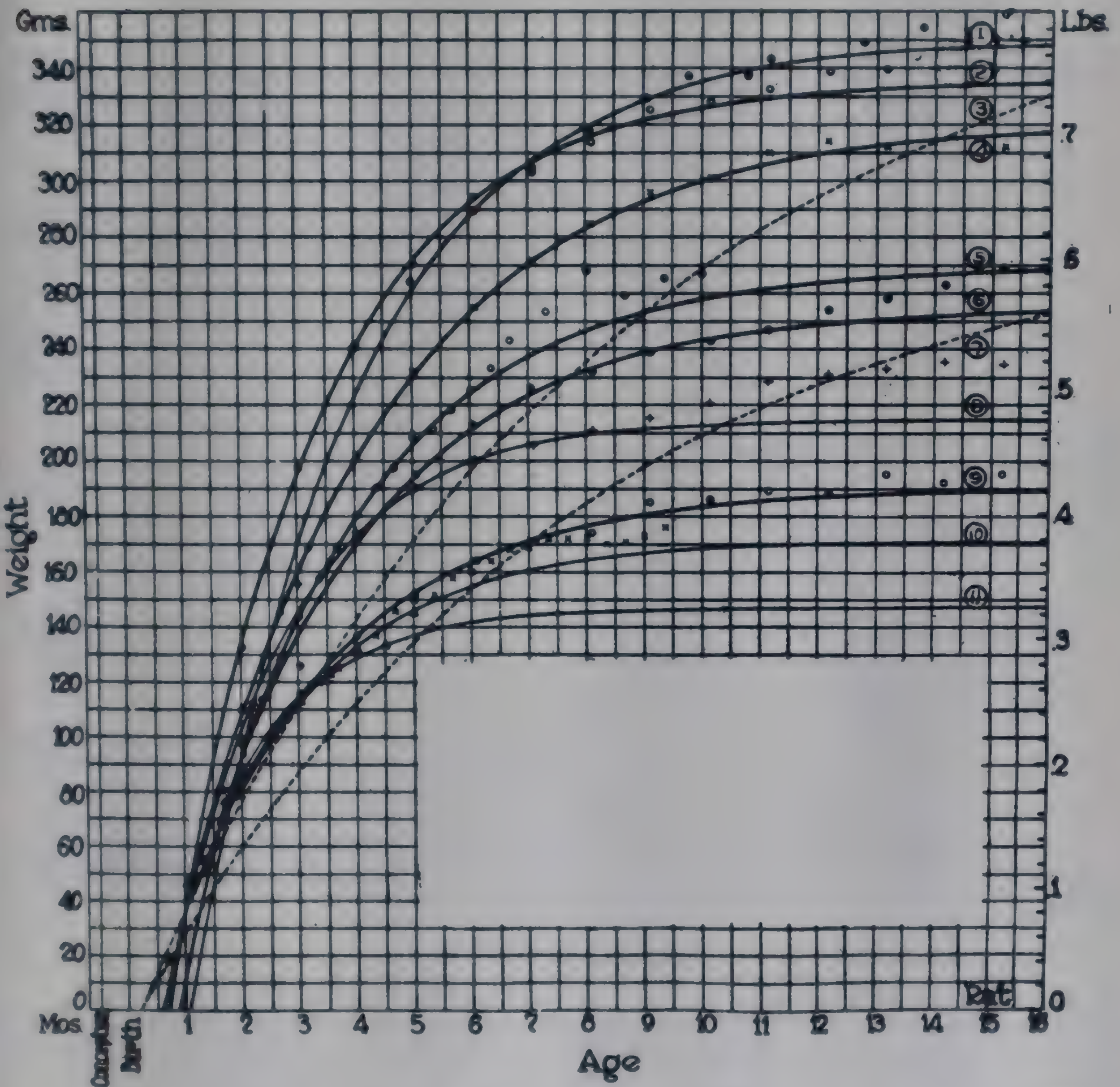
which indicates that the fraction of the mature weight, W/A, is a function of the product of the velocity constant, k, and the age as counted from t^*.

When B is known, t^* may be computed as follows:

When $t = t^*$, $W = 0$; therefore

$$0 = A - Be^{-kt^*} \qquad \ln A = \ln B - kt^*$$

$$A = Be^{-kt^*} \qquad t^* = \frac{\ln B - \ln A}{k} \tag{15}$$



	k	A	t^*	*Sex*	*Notes*	*Source*
1.	.350	350	1.76	♂		Greenman
2.	.333	335	1.4	♂	7–15 Generations	King
3.	.122	385	.9	♂	Norway	King
4.	.291	320	1.3	♂	16–25 Generations	King
5.	.341	270	1.6	♂		Ferry
6.	.330	255	1.38	♂	Controls	King
7.	.13	290	.20	♀	Norway	King
8.	.48	215	1.4	♀	7–15 Generations	King
9.	.357	189	1.28	♀	Controls	King
10.	.418	172	1.12	♀		Ferry
11.	.621	147	1.3	♀	Runt	King

Fig. 16.46. Growth of rats.

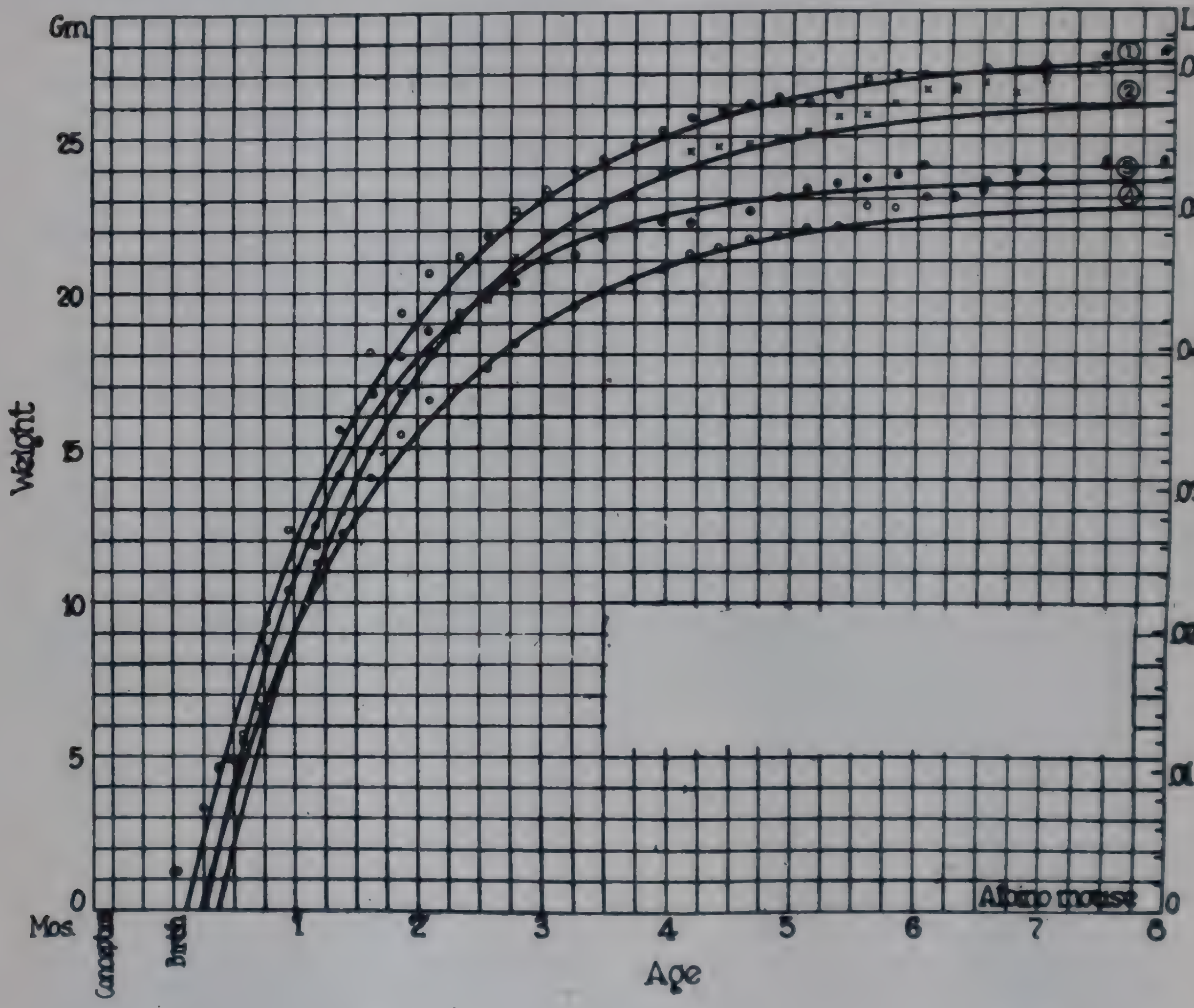
It is often desirable to know the ages when given weights, or given fractions of the mature weights, are reached. These may be determined as follows:

$$A - W = Be^{-kt} \tag{11}$$

$$\ln(A - W) = \ln B - kt$$

$$kt = \ln B - \ln(A - W)$$

$$\therefore\ t = \frac{\ln B - \ln(A - W)}{k} \tag{16}$$



	A	*k*	*t**	*Sex*	*Source*
1.	275	−.62	.76	♂	Robertson, 1916
2.	260	−.672	1.03	♂	Robertson and Ray, 1925
3.	235	−.82	.92	♀	Robertson
4.	228	−.639	.88	♀	Robertson and Ray

Fig. 16.47. Growth of mice.

A further simplification may be introduced. Assuming that it is desired to determine the age when some fraction, such as 90 per cent of the mature weight, is reached, W may be replaced by $0.9A$, and equation (16) becomes

$$t = \frac{\ln B - \ln(A - 0.9A)}{k}$$

$$= \frac{1}{k}\,(\ln B - \ln 0.1A)$$

or in general,

$$t = \frac{\ln B - \ln\left(1 - \frac{W}{A}\right)}{k} \tag{17}$$

For linear growth B may have the same numerical value as A, and equation (12) becomes

$$W = A - Ae^{-kt} = A(1 - e^{-kt}) \tag{12a}$$

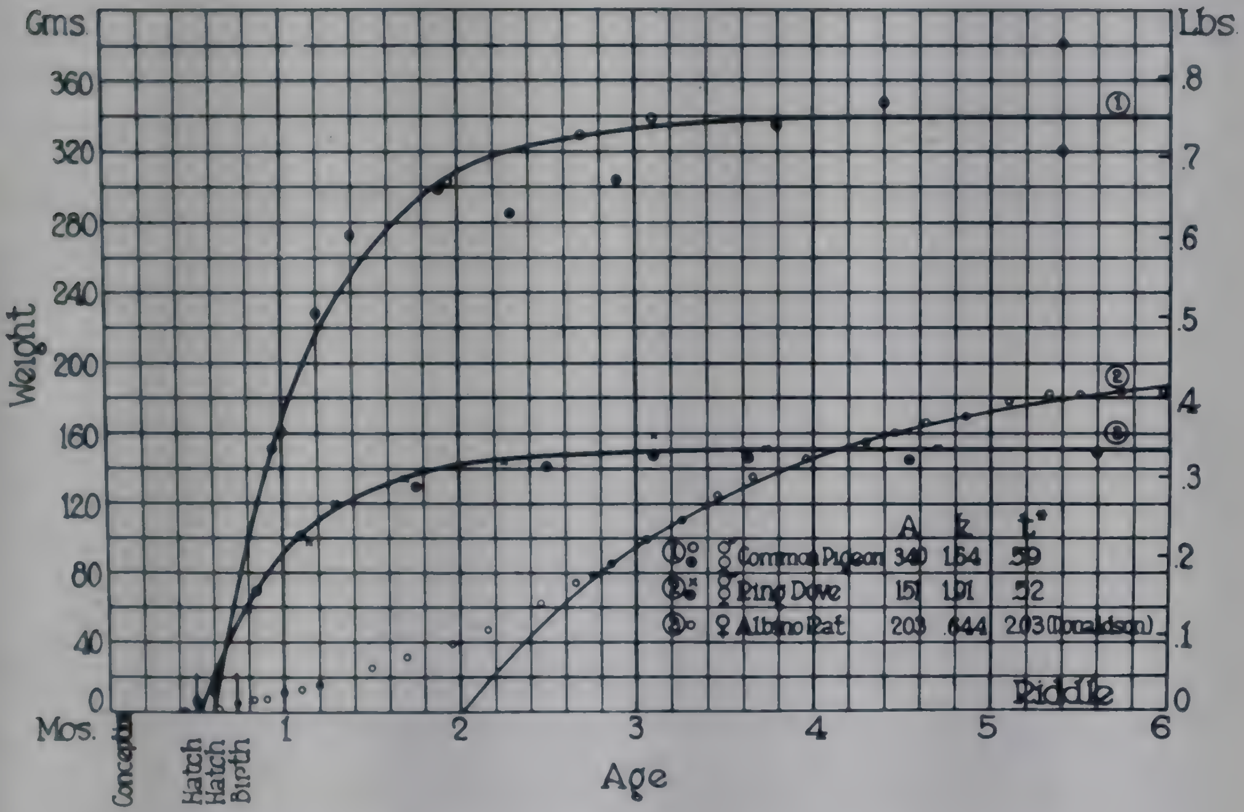


Fig. 16.48. Growth of pigeons, doves (Riddle) and rats.

Equation (12a) offers a simpler method of determining the weight at a given age. From (12a)

$$\frac{A - W}{A} = \epsilon^{-kt}$$

$$\ln \frac{(A - W)}{A} = -kt$$

$$t = -\frac{1}{k} \ln \frac{(A - W)}{A} = -\frac{1}{k} \ln\left(1 - \frac{W}{A}\right) \tag{17a}$$

Equation (17a) shows that, when the value of k is known, one can easily determine the age at which a given fraction of the mature weight is reached. Thus if it is desired to determine the age at which half of the mature weight is reached, W is replaced by $0.5A$, and

$$t = -\frac{1}{k} \ln\left(1. - \frac{0.5A}{A}\right) = -\frac{1}{k} \ln 0.5 = \frac{0.69315. \ . \ . \ .}{k}$$

In a similar manner, the age when any other fraction of the mature weight is reached may be found by substituting the desired value in equation (17a). The following table, in which a series of numerical values of natural logarithms of $\left(1 - \frac{W}{A}\right)$ are given, facilitates numerical computations.

Equation (14) may similarly be used for evaluating the age when a desired fraction of the mature weight is reached.

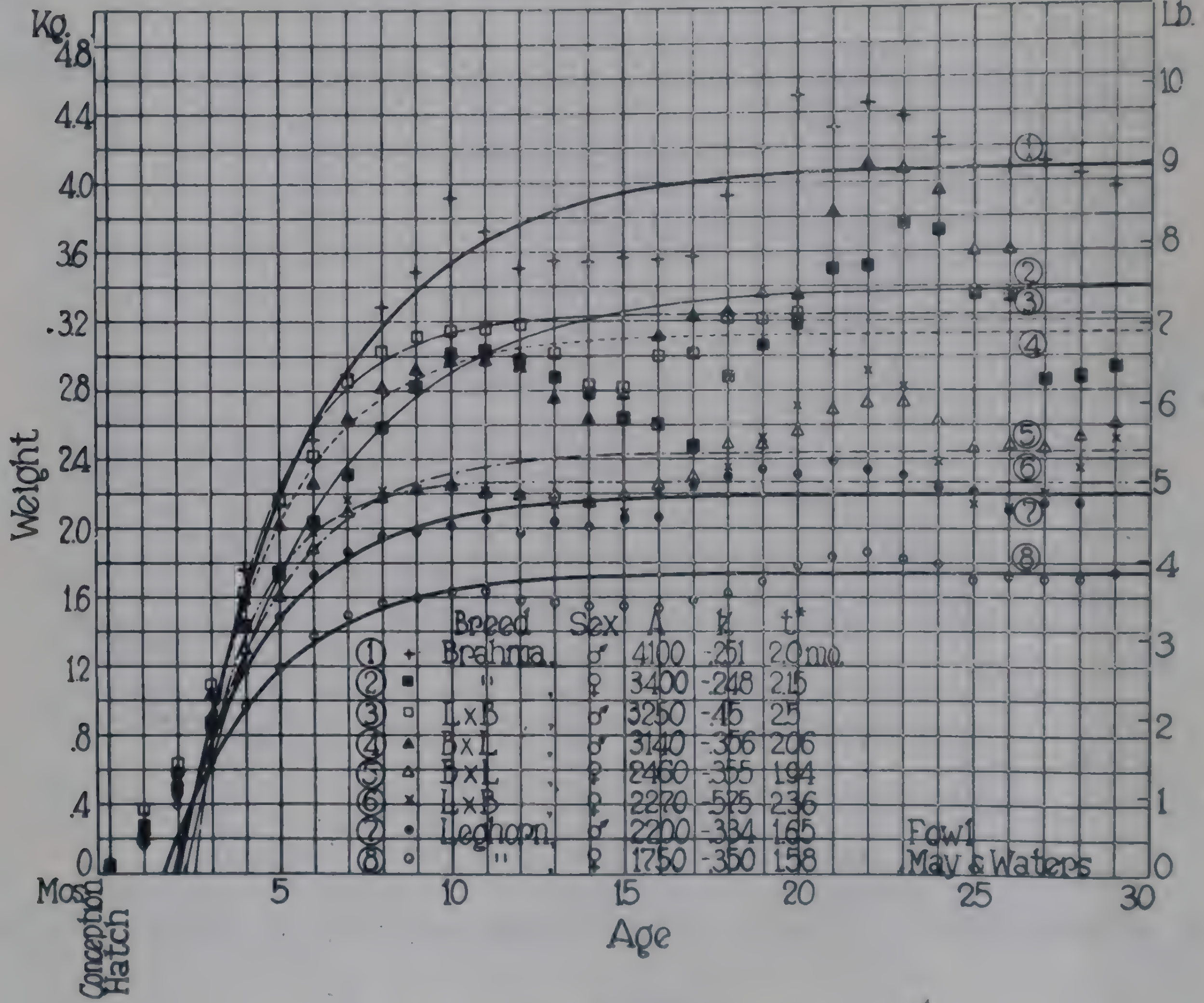


Fig. 16.49. Growth of domestic fowl.

$$\frac{W}{A} = 1 - e^{-k(t-t^*)} \qquad 1 - \frac{W}{A} = e^{-k(t-t^*)} \tag{14}$$

$$\ln\left(1 - \frac{W}{A}\right) = -k(t - t^*) \qquad t = t^* - \frac{1}{k}\ln\left(1 - \frac{W}{A}\right) \tag{18}$$

t is easily determined when k and t^* are known. Thus if it is desired to find the age, t, when half of the mature weight is reached, W is replaced by $0.5A$:

$$t = t^* - \frac{1}{k}\ln 0.5 = t^* + \frac{0.69315}{k}$$

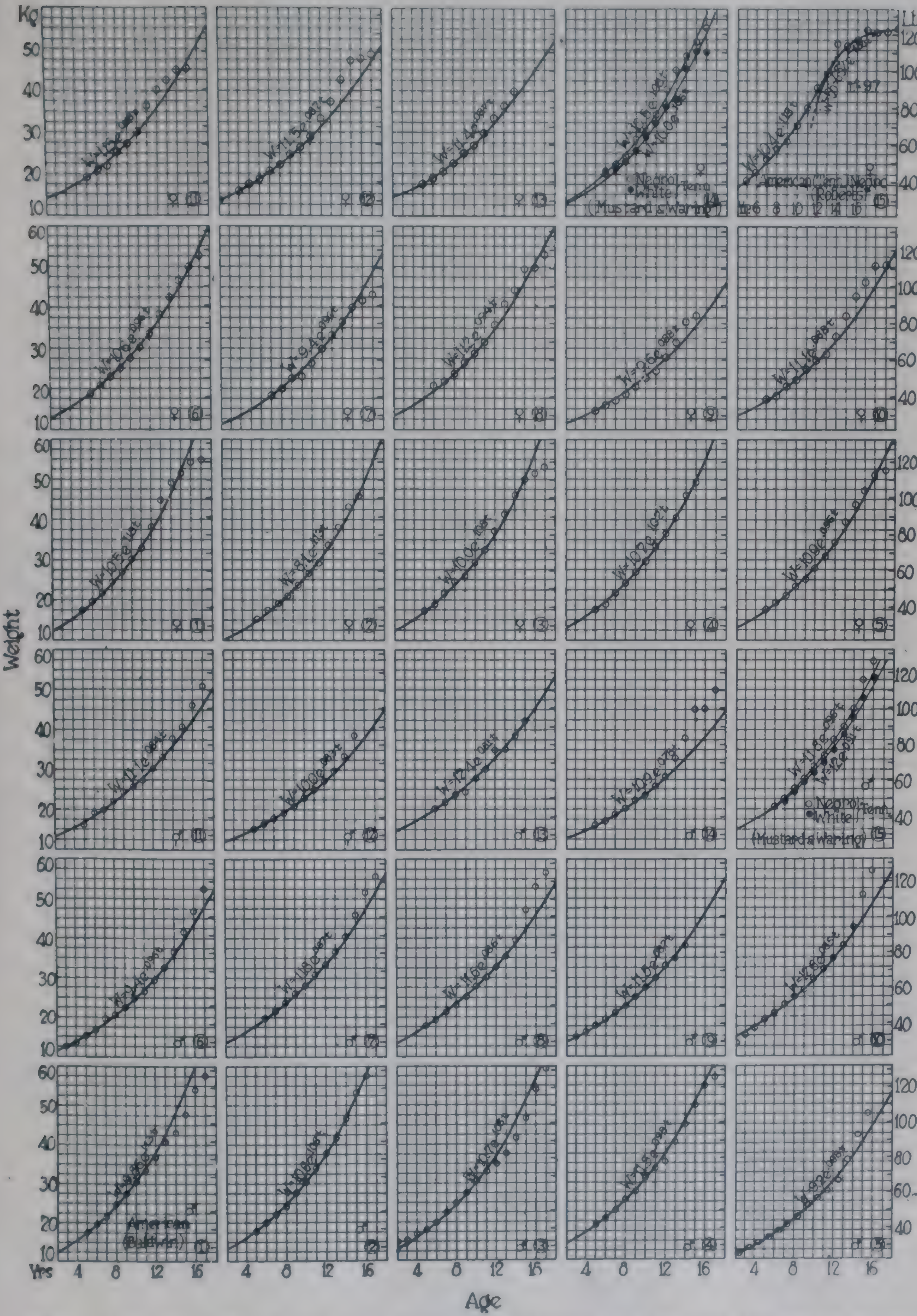


Fig. 16.50. Growth of children preceding puberty (16.50) and following puberty (16.51). Note the considerable differences in mature weights and in the shape of the age curves in these figures as also in Figs. 16.52 to 16.54, probably due to differences in environmental conditions.

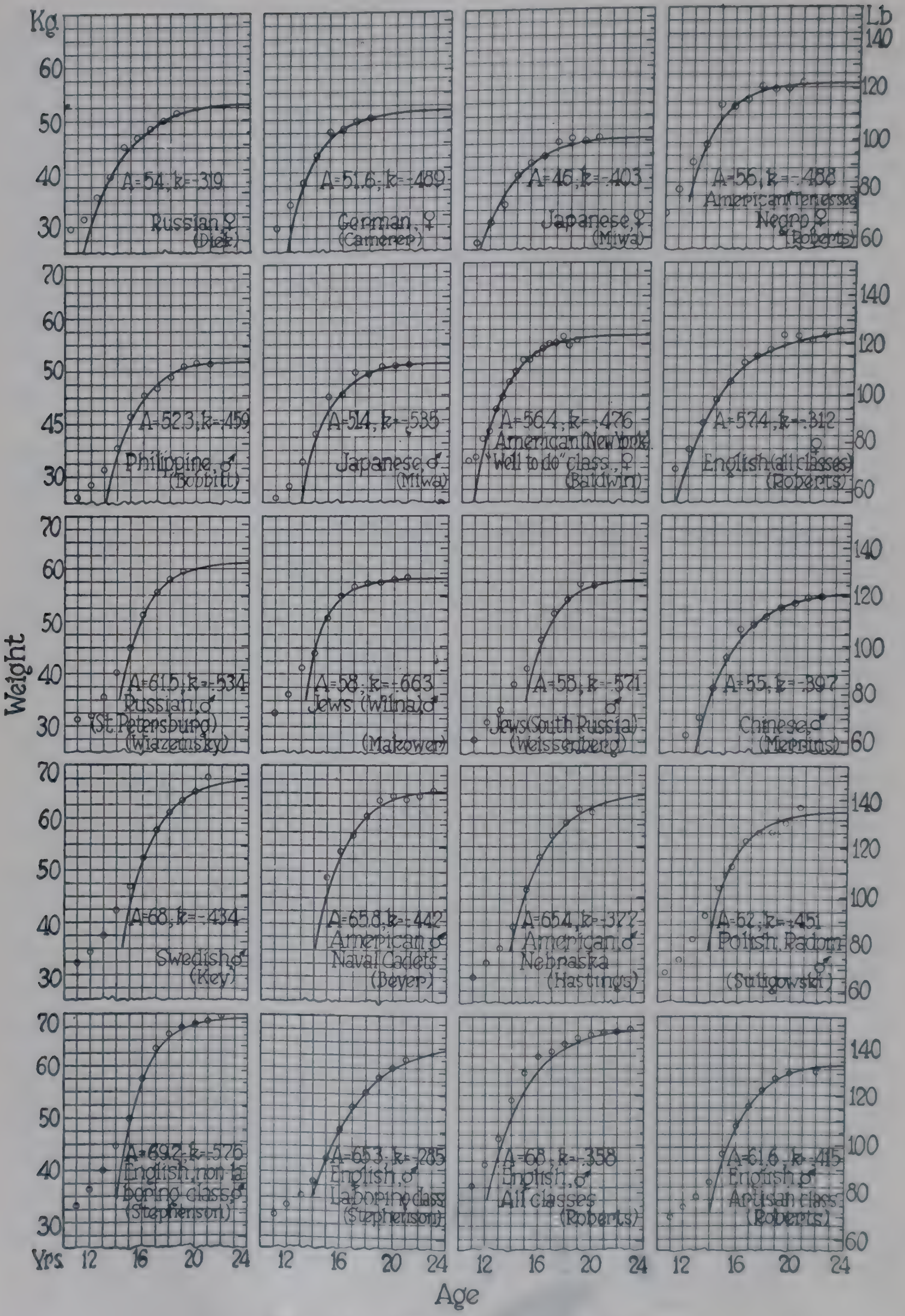


Fig. 16.51. See legend for Fig. 16.50.

TABLE TO FACILITATE ESTIMATING AGES AT WHICH DIFFERENT FRACTIONS OF THE MATURE WEIGHT ARE REACHED

Fraction of Mature Weight $\left(\frac{W}{A}\right)$	$\ln\left(1-\frac{W}{A}\right)$	Fraction of Mature Weight $\left(\frac{W}{A}\right)$	$\ln\left(1-\frac{W}{A}\right)$
0.25	−0.28768	.70	−1.2040
.30	−0.35667	.75	−1.3863
.35	−0.43078	.80	−1.6094
.40	−0.51083	.85	−1.8971
.45	−0.59784	.90	−2.3026
.50	−0.69315	.95	−2.9957
.55	−0.79851	.98	−3.9120
.60	−0.91629	.99	−4.6052
.65	−1.0498	.999	−6.9078

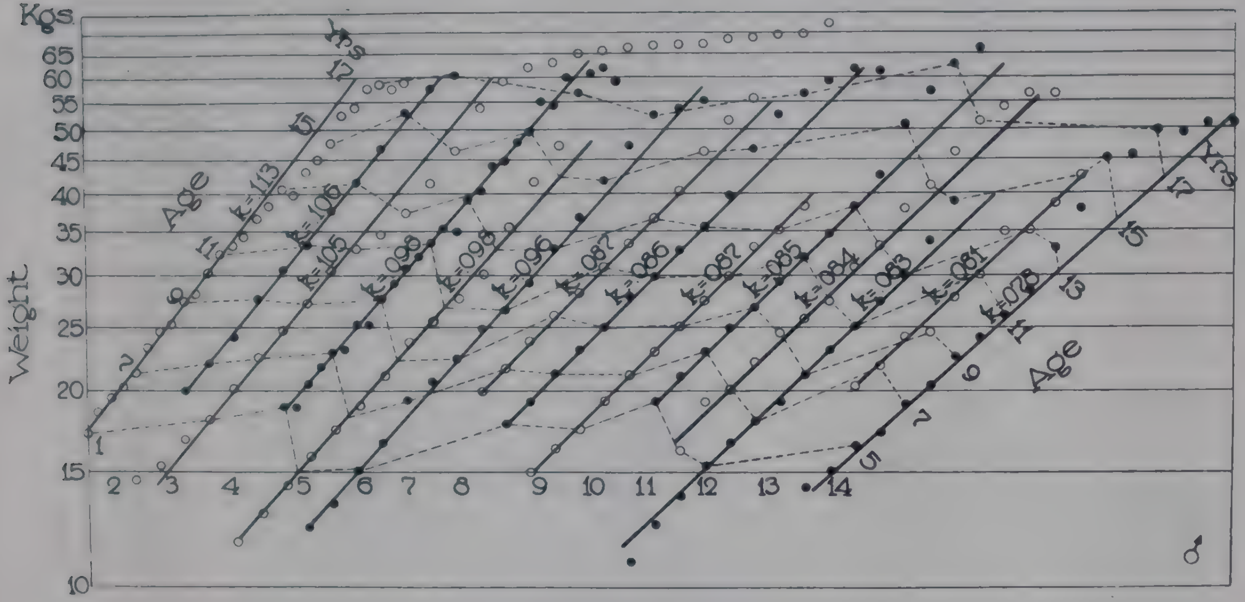


Chart for boys

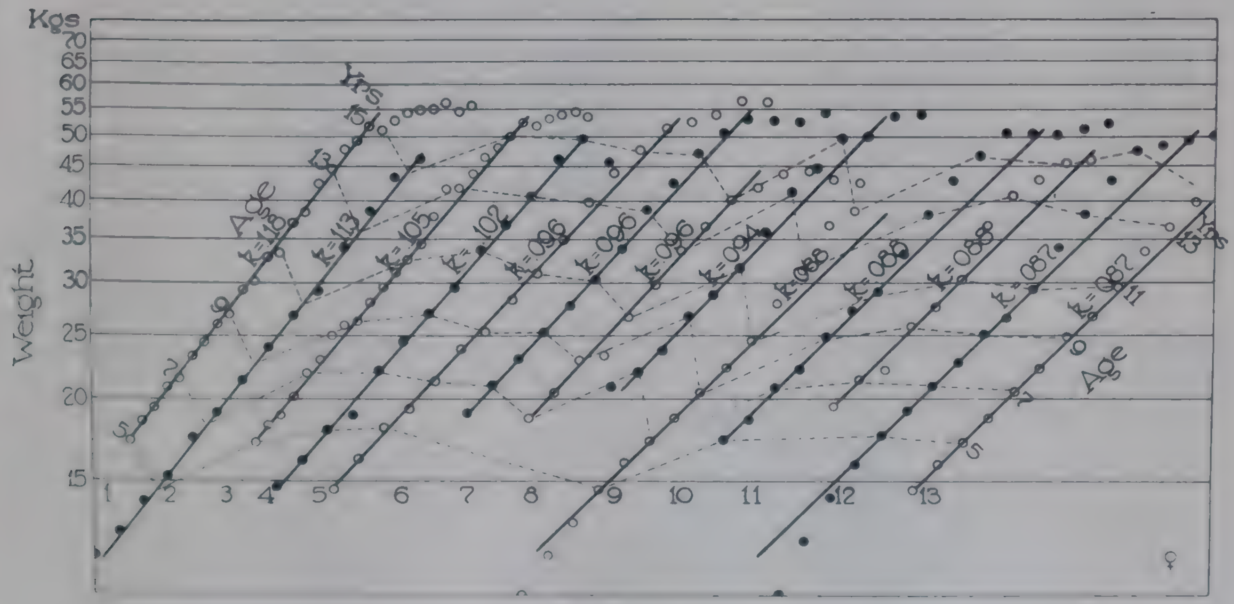


Chart for girls

Fig. 16.52. The juvenile course of growth of children (same data as in Fig. 16.50) plotted on an arithlog grid. It appears that the "pubertal acceleration" represents compensating growth in children who were relatively under nourished during the earlier years, because Fig. 16.52 indicates that the lower the value of k (percentage growth rate) the greater the pubertal acceleration.

The following transformation of equation (14) gives a straight-line function for the growth curve. Transforming

$$1 - \frac{W}{A} = e^{-k(t-t^*)}$$

$$\ln\left(1 - \frac{W}{A}\right) = -k(t - t^*)$$

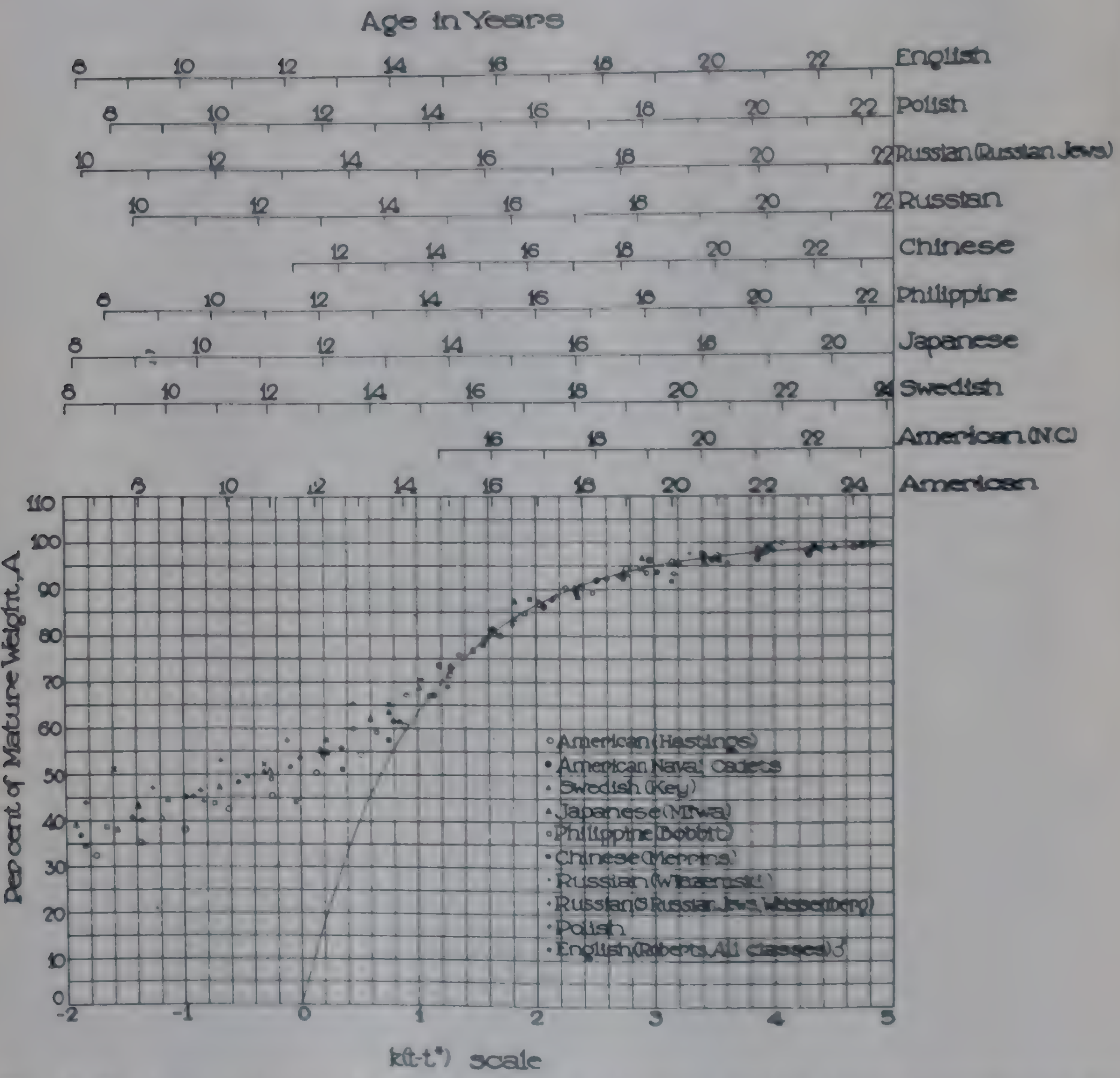


Fig. 16.53. A comparison of growth curves of children, males, during the post-pubertal period.

This means that plotting values of $\left(1 - \frac{W}{A}\right)$ (which is the fraction of growth yet to be made to reach the mature weight) against age t or $(t - t^*)$ on arithlog paper results in a straight line having the slope k. Fig. 16.28 illustrates the method. This derivation could be foreseen in connection with the method of evaluating A, which consisted in plotting $(A - W)$ against age. This method merely places the curve on a percentage basis.

k (and also B) may be determined from the curve obtained by plotting the velocities of growth against age.

$$W = A - Be^{-kt} \tag{12}$$

$$\frac{dW}{dt} = kBe^{-kt} = Ce^{-kt}$$

$$\ln \frac{dW}{dt} = \ln kB - kt.$$

Hence, plotting the velocities $\frac{dW}{dt}$ (or in practice the successive increments per unit time) against the corresponding ages on arithlog paper will result in a straight line having the slope k. This method is inferior to plotting $(A - W)$ against age on account of fluctuations due to experimental errors.

The fact that the numerical value of the velocity constant, k, is the same in the differential and integral equations makes it possible to derive equation (12) from a knowledge of growth velocities (*i.e.*, gains in weight per unit time at successive ages).

$$W = A - Be^{-kt} \tag{12}$$

$$\frac{dW}{dt} = kBe^{-kt} = Ce^{-kt}$$

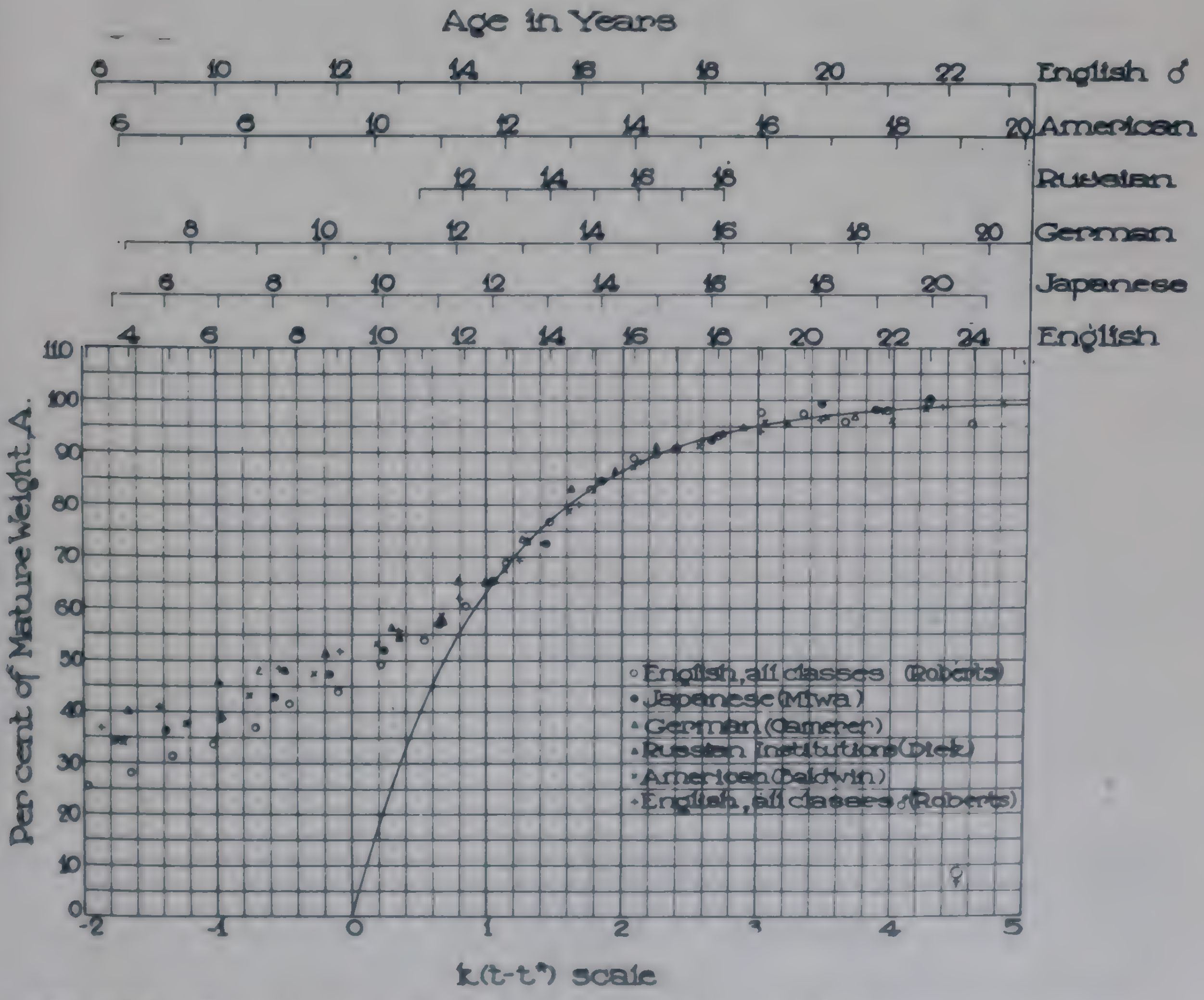


Fig. 16.54. Growth curve of children, females, during the post pubertal period.

Integrating the last equation,

$$W = \frac{Ce^{-kt}}{k} + A \text{ (integration constant).}$$

$$\text{When} \quad t = \infty, \quad W = A.$$

$$\text{When} \quad t = 0, \quad W = A - \frac{C}{k} = A - B.$$

Therefore

$$W = A - Be^{-kt} \tag{12}$$

Thus it is possible to begin with equation $\frac{dW}{dt} = Ce^{-kt}$

in place of $\frac{dW}{dt} = k(A - W)$

and obtain the same result.

For other properties of the growth equation, see Chapter 19.

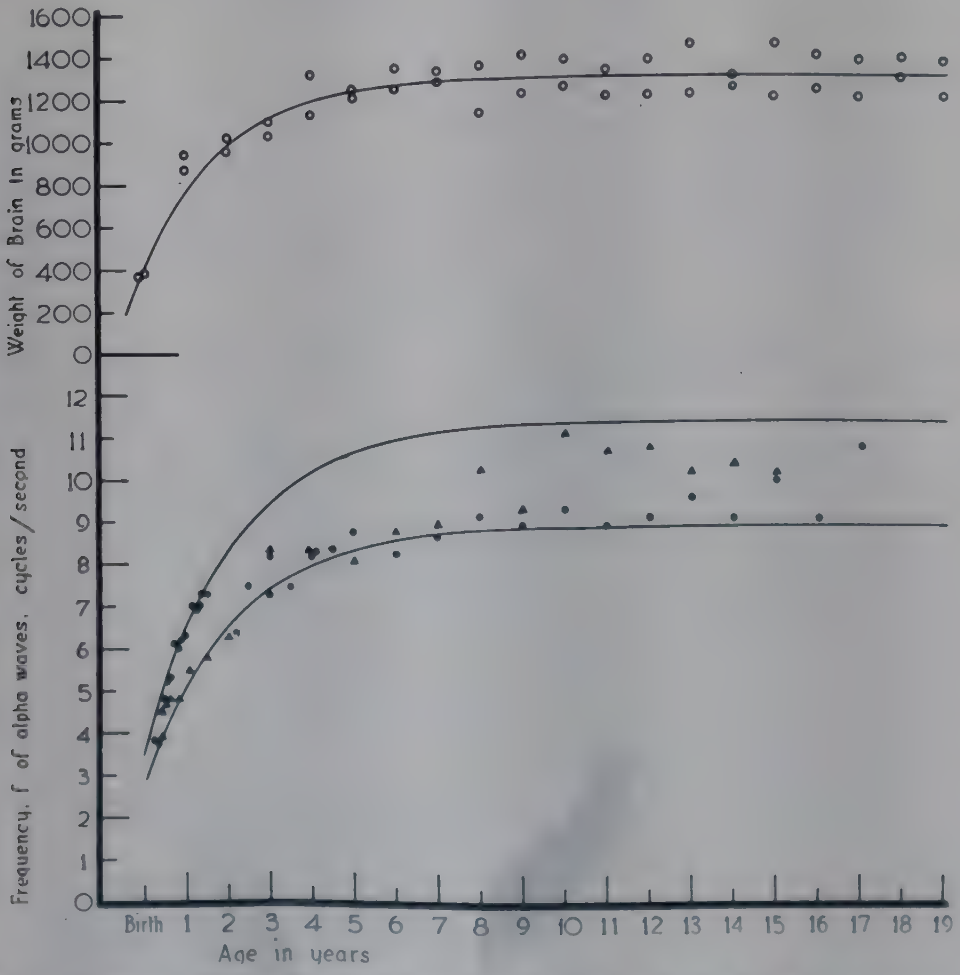


Fig. 16.55a. Growth of the human brain in weight, W, and in frequency, f, of brain potentials (or alpha frequency or alpha waves, or Berger rhythms). The value of $-k$ (decline in the relative growth rate) is -0.468 for the alpha waves and -0.485 for brain weight (*i.e.*, 48.5 per cent per year); the mature values, W_A and f_A are 1333 gm. for the brain and 10 for the alpha waves. Since $\frac{W}{W_A} = \frac{f}{f_A} = W = f\frac{W_A}{f_A}$; that is, the brain weight, W, is 133.3 times the alpha wave frequency, f (Weinbach).

Summarizing this discussion, prior to puberty in animals, flowering in plants, and "coming of age" in populations, the growth rate tends to be proportional to the growth already made, indicated by the equation

$$\frac{dW}{dt} = kW \tag{5}$$

$$W = Ae^{kt} \tag{8}$$

Following this age growth rate tends to be proportional to the growth yet to be made

$$\frac{dW}{dt} = -k(A - W) \tag{9}$$

$$W = A - Be^{-kt} \tag{12}$$

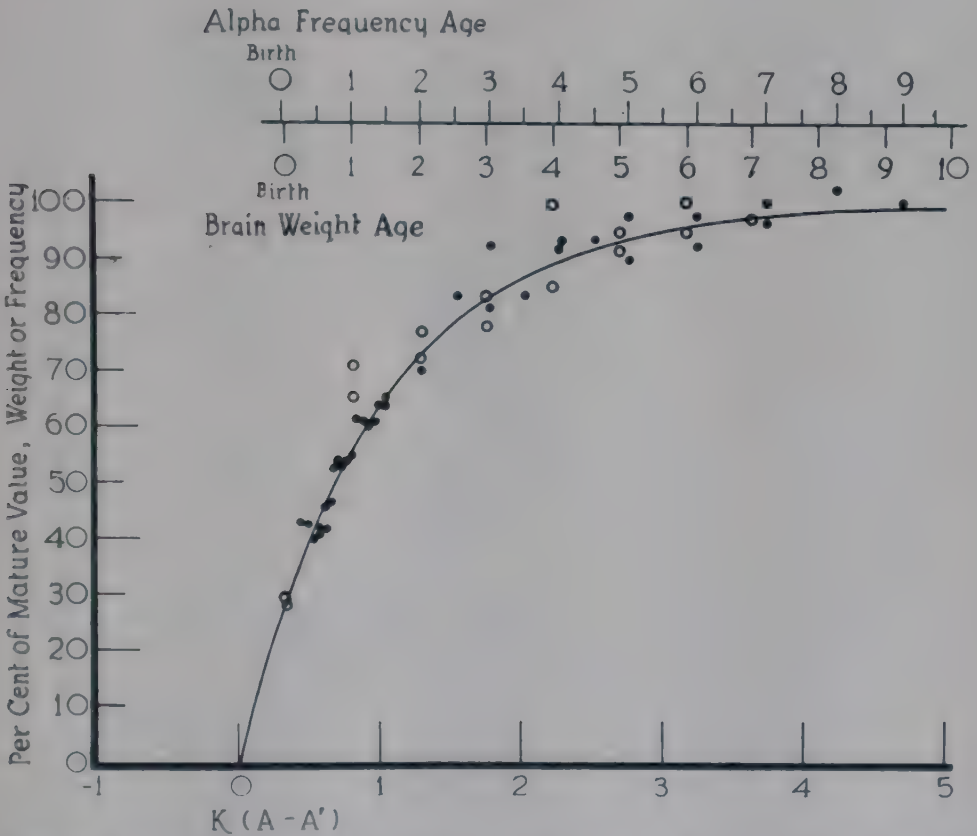


Fig. 16.55b. The equivalence chart between brain and wave frequency shows their excellent correspondence. Courtesy of A. P. Weinbach, *Growth*, **2**, 247 (1938).

[The numerical value of k in equation (9) or (12) is, of course, different and has an opposite sign from the k in equation (5) or (8)].

Animals rapidly attaining the maximal body weight, A, have a high slope, k, as in equations (9) or (12); those attaining it slowly, have a low slope, k. The value of k for given guinea pigs is 0.22; for cattle, which approach mature weight much more slowly, the value of k is much lower, 0.04; for mice, approaching the mature weight much more rapidly, k is much higher, 0.71; and so on.

16.6: Genetic growth constants. The value of A (mature weight) and of the slope, k, on the growth curve are intrinsic or genetic characteristics of the animal under given environmental conditions, in the same sense that the equilibrium and velocity constants of a chemical reaction *in vitro* are intrinsic characteristics of the chemical system under given conditions. Growth, like a chemical reaction *in vitro,* is by definition increase in the mass of one component at the expense of another, and the rates of approach to the equilibrium level are analogous. Table 16.1 (appendix) presents numerical values of the intrinsic or genetic growth constants, A, k, and related derived values. Figs. 16.30 to 16.54 present the constants graphically, together with age curves of growth in weight of several animal species.

The charts are for the most part self-explanatory. The values of A (mature weight), k (speed of approach to mature weight during the self-inhibiting phase of growth), and t^* (age at which the extrapolated curve meets the age axis) are given for each species. The differences within the species are due mostly to differences in environmental conditions, especially food supply.

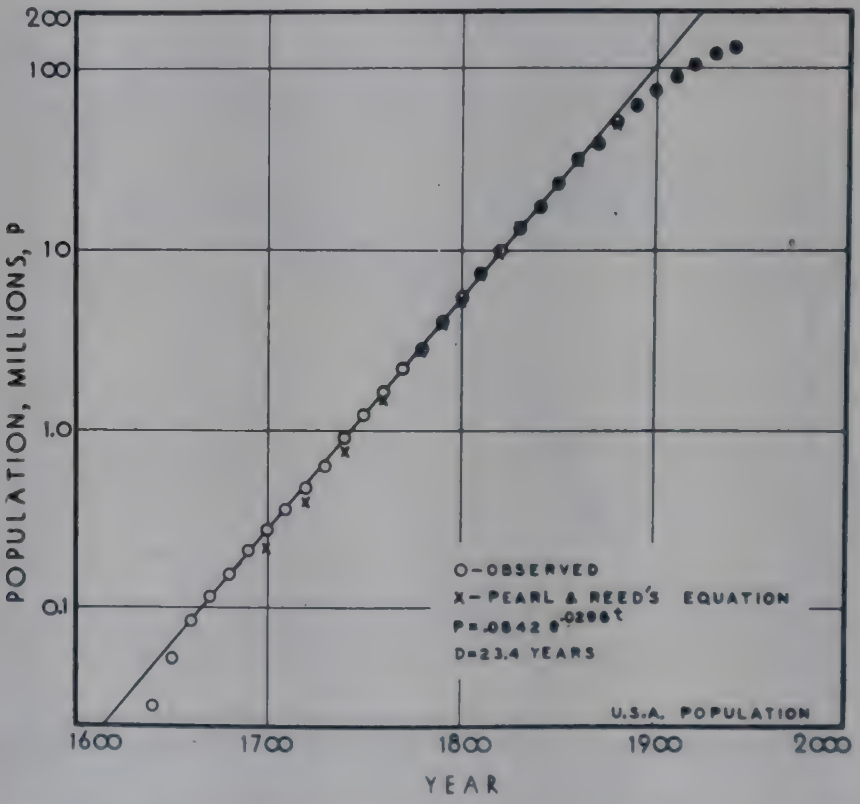


Fig. 16.56a. The growth of the human population in the U.S.A., plotted on semilog paper. The line represents the equation $P = .0842e^{0.029t}$, meaning that the population, P, grows at 2.9% per year (instantaneous basis) or is doubled in 23.4 years.

Before proceeding with the discussion of the influence of environment on the numerical values of the constant, it is interesting to note that the mature size, A, of different species tends to be related to the growth constant, k, or to the time required to reach a given percentage of the mature weight (Fig. 16.29 plotted from Table 16.1). As might be expected from the long juvenile period, the data points for man deviate from the general curve. Also, as might be expected, there is considerable scatter of the data because A and k are not influenced by environmental conditions in the same direction and the environmental conditions for the different animals were not the same. Moreover, males, females, and castrates were lumped together in Fig. 16.29. Nevertheless, the index of correlation is relatively satisfactory.

We may begin by pointing to the difference in approach to mature weight in Wistar Norway and albino rats[30] (Fig. 16.30). The mature weight is virtually the same in both, but the albinos attained mature weight much earlier. Dr. King informed us that the Norway curves approach the albinos with successive generations of cage life. Cage life apparently does not agree with first-generation Norway rats.

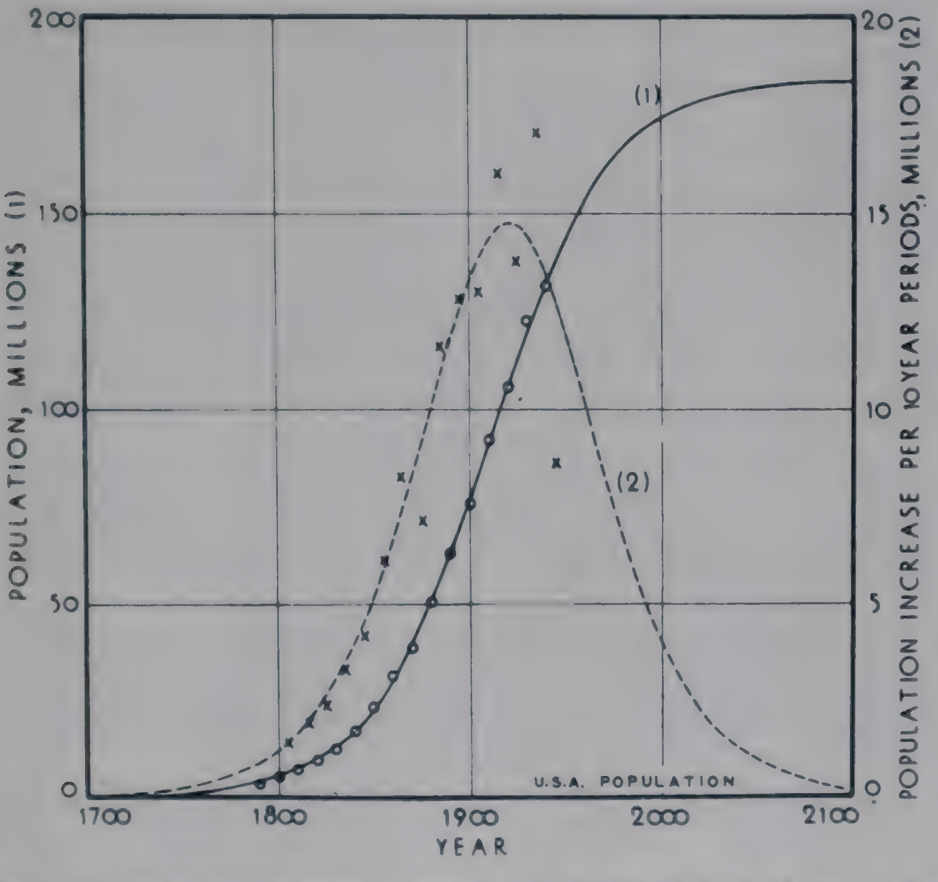


Fig. 16.56b. Growth of the human population in the U.S.A. showing the increment curve (2) and cumulative curve (1), extrapolated to year 2100.

Figs. 16.31 and 16.32 represent growth curves of albino rats fed on ordinary and "improved" diets. The animals on the "maximum-growth" ration reach the mature size much earlier than the controls. The data for Osborne and Mendel "maximum growth" rats were given the writer by Dr. Osborne during a personal visit. Many published papers from Osborne and Mendel's laboratory on exceptionally rapid growth of rats[31] substantiate the curves in Fig. 16.31 and 16.32.

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[30] Data in Donaldson, H. H., "The rat," 1915, 1924 (Wistar Institute, Philadelphia).

Similar results were observed on other species. Thus, Figs. 16.33 and 16.34 indicate that the average English "laboring" individual appears to be smaller than the average "non-laboring" individual, and that children of the laboring class take longer to reach a given growth stage than those of the non-laboring. This difference may be due in part to differences in environmental conditions.[32] This difference in weight-growth rate (see also Figs. 16.50 to 16.54) may partially account for differences in intelligence quotients. It is not unreasonable to assume that mental and physical development are associated.[33]

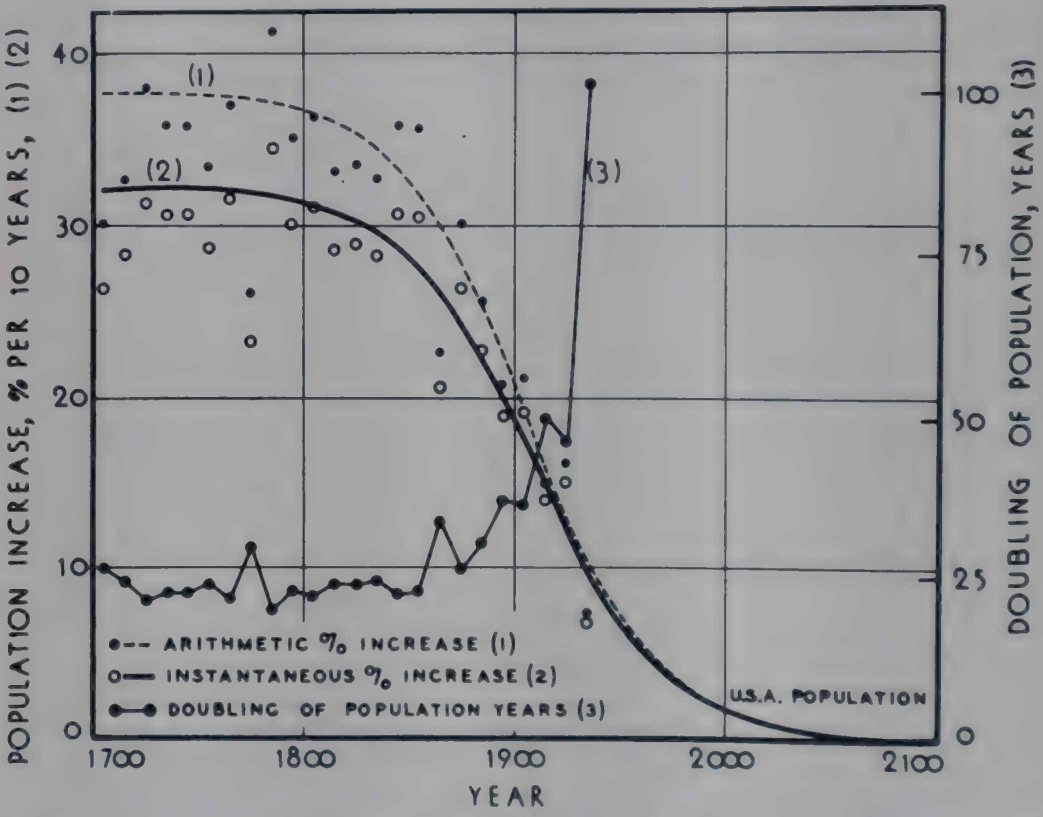

Fig. 16.56c. Percentage increase (1 and 2) in and time required for doubling human population in the U.S.A. (3).

Since the maintenance cost of animals is the largest item in the growth cost, rapid growth and early maturity imply some saving, and therefore increased efficiency not only of growth but also of productive processes (such as milk and egg production, muscular work), since the growth expense is charged to the productive process during maturity. (For exceptions, see Chs. 3 and 18.)

There are similar environmental influences on the maturation speed of physiological functions, such as milk production, illustrated in Figs. 16.35 to

[31] Osborne, T. B., and Mendel, L. B., *et al.*, *J. Biol. Chem.*, **69,** 611 (1926), and **75, 776** (1927). Smith, A. H., and Bing, F. C., *J. Nutrition*, **1,** 179 (1928–29). Anderson, W. E., and Smith, A. H., *Am. J. Physiol.*, **100,** 511 (1932). Bryan, A. H., and Gaiser, D. W., "Diet and pituitary hormone on growth," *Am. J. Physiol.*, **99,** 379 (1931–32).

[32] *Cf.* Paton, D. N., and Findlay, L., "Poverty, nutrition and growth," Medical Research Council (English) Special Report 101, 1926.

[33] *Cf.* Biehl, W. C., "Early inanition and the developmental schedule in the rat," *J. Comp. Psychol.*, **28,** 1 (1939).

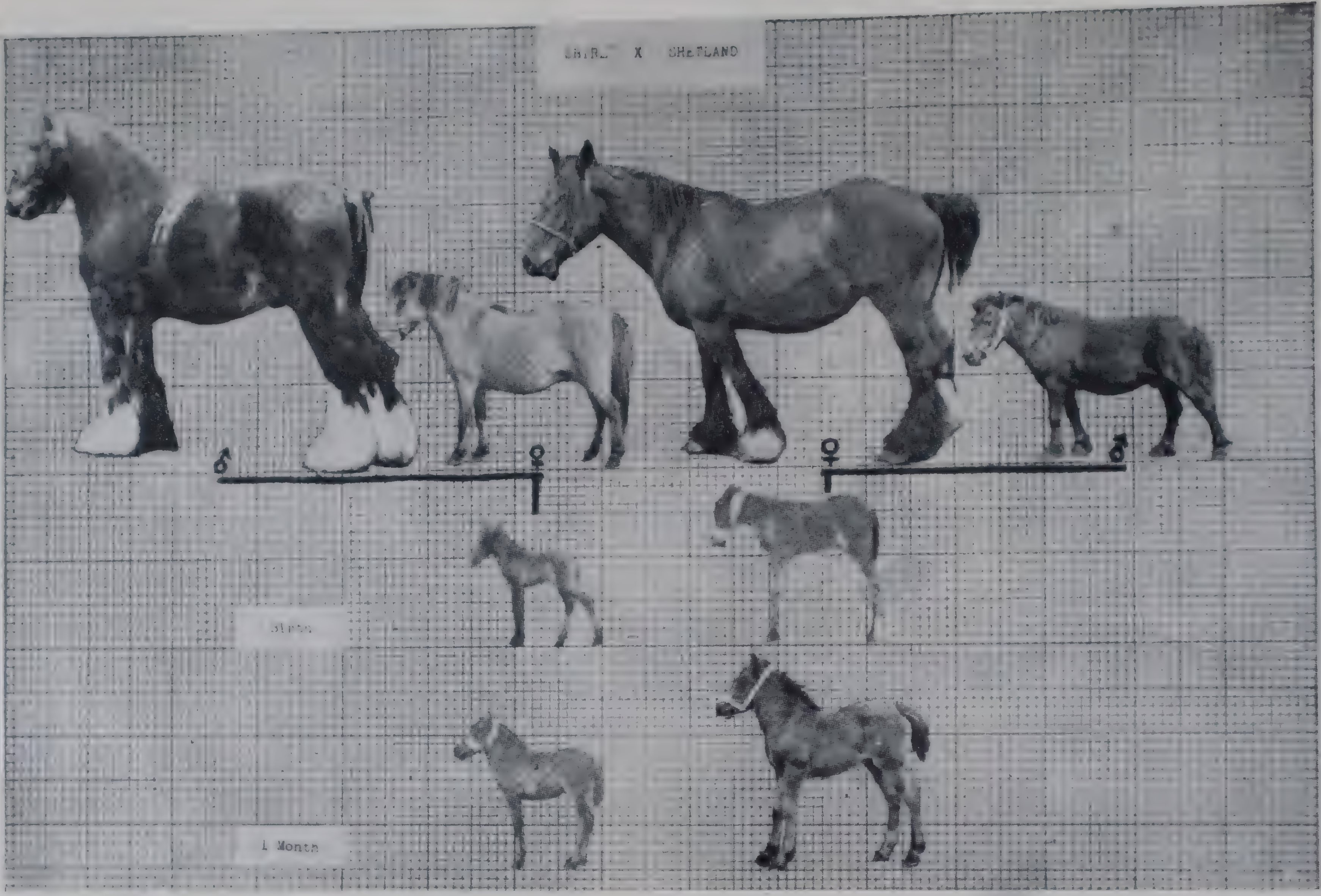

Fig. 16.57. Parents and offspring of reciprocal Shetland-Shire crosses. Courtesy of Arthur W. Walton and John Hammond, *Proc. Roy. Soc. London*, **125B**, 311 (1938).

16.38. Advanced Registry dairy cattle receive better care and feed, and they approach their maximum milk yield and weight at an earlier age.

Employing chemical terminology, increasing the effective concentration of the growth-limiting constituents (food) in the system increases the velocity, k, of the process (growth). The growth velocity, k, of the poorly fed rat of Donaldson (Figs. 16.31 and 16.32) is 0.0135, but that of the well-fed rat of Osborne and Mendel is 0.0266; thus the speed of approach to the mature value is twice as great in the rats on the better diet.

Nutritional aspects of growth are discussed in Chapter 20; endocrine aspects, in Chapter 7; seasonal aspects, in Chapter 8; temperature aspects, in Chapter 11.

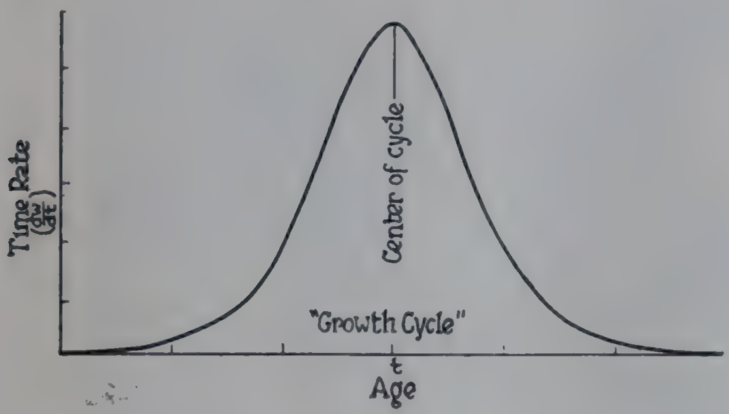

Fig. 16.57a. Robertson's theoretical autocatalytic monomolecular cycle representing the time rate of gain, dW/dt, as function of time. Note its symmetry about the center. Actual "growth cycles" are not so symmetrical.

Fig. 16.57, from Walton and Hammond,[34] is a dramatic illustration of spatial effect on growth—how the size of the mother influences the prenatal size of the offspring. The parents were the giant (1800 – 2400-lb or 800 – 1000-kg) Shire and the dwarf (540-lb or 200-kg) Shetland. The cross foals from the giant mother and dwarf father were three times the size of the cross foals from the dwarf mother and the giant father. The maternal-environmental limitation masked the genetic differences during the prenatal period of growth. After weaning, however, the genetic influence came into its own. The cross foals of the dwarf mothers grew much more rapidly than Shetlands and the growth curves of the two crosses tended to converge to a common mature weight. Byerly[35] reported similar results by hybridizing bantam silkies and Rhode Island Red chickens.

16.7: Note on the relation between average and individual growth curves. A fundamental characteristic of living organisms is that they are alike in general plan and different in detail. There are two corresponding schools of biologists, one of which emphasizes the average and general and the other the individual and particular. The rapid development and diffusion of statistical techniques in the biologic as well as in the physical sciences tends to emphasize average and the general; on the other hand, great discoveries and

[34] Walton, A., and Hammond, J., *Proc. Roy. Soc. London*, **125B**, 311 (1938), and in several other publications.

[35] Byerly, T. C., *et al.*, *J. Exp. Zool.*, **78**, 210 (1938).

concepts of biology have resulted from scrutiny of the individual, of the detail. Thus the concept of natural selection emphasized differences between individuals; the notion of gene is an individual one; so is the concept of mutation. Both approaches are useful, depending on the opportunities and aims.

Davenport[36] investigated the relative significance of individual and average growth curves of children with special reference to the adolescent growth spurt. He found that adolescent growth acceleration is often explosive, occurring at any time between 11 and 17 years. It may be sharp or fluctuating, high or low. Environment could not be the chief factor because great variations were observed between brothers reared in the same home.

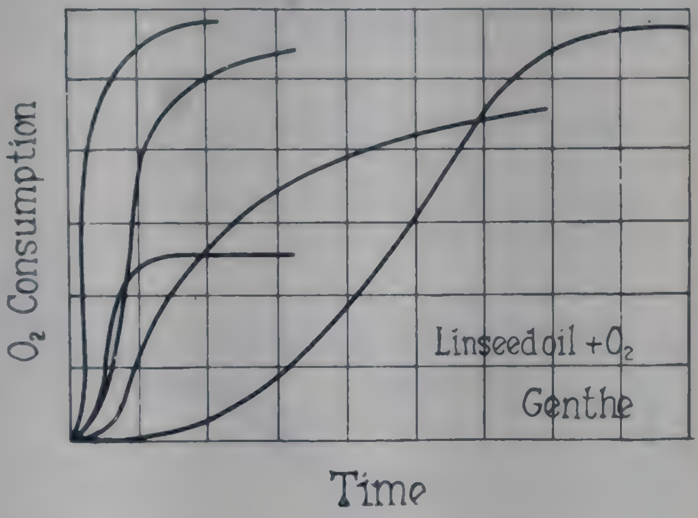

Fig. 16.57b. The time course of oxidation of linseed oil under various conditions, a familiar autocatalytic process resembling growth curves.

Davenport believes that the average increment curve not only resembles the Gaussian (probability) distribution curve, but is a Gaussian curve. The peak of the average increment curve is at 14.5 years; individual growth spurts are distributed around this average. The frequency and amplitude of the spurts diminish on each side of the peak. Similar results were reported by Boas,[37] Gray,[38] and others (Fig. 16.60a). Merrell[39] reached a similar conclusion for rabbits. The Pearl-Reed logistic was fitted to individual and average growth curves of rabbits. The average differed in fundamental characteristics from the separate curves. Significant undulations observed in the average were absent in the individual growth curve. Undulations and changes in skewness are often the result of the averaging process, unrelated to the biology of growth. In brief, the growth process in an individual is not the smooth sigmoid curve represented by average curves. The average curve represents properties of the mathematical averaging process often absent in individuals. A considerable literature is being developed on individual growth by the "longitudinal" method consisting of seriatim observations[40] of the same individuals.

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[36] Davenport, C. B., *Proc. Am. Philosop. Soc.*, **70**, 381 (1931).
[37] Boas, F., *Science*, **72**, 44 (1930).
[38] Gray, A. H., *Roy. Phil. Soc. Glasgow*, **40**, 139 (1909).
[39] Merrell, M., *Human Biology*, **3**, 37 (1931).
[40] Scammon, R. E., "Seriatim study of human growth," *Am. J. Physical Anthrop.*, **10**, 329 (1927).

16.8: Growth of the human population in the United States.

> In the next 25 years the population of the Island will be 28 million, and the means of subsisence only equal to the support of 21 million. In the next period, the population would be 56 million, and the means of subsistence just sufficient for half that number. *T. R. Malthus,* 1798.

It may be surprising to learn that the growth of the human population has the same shape and may be represented by the same equations as the growth curves of individual animals and of populations of bacteria, yeast, and flies confined to a limited space. Yet this appears to be true, and attention has already been called to this similarity (Figs. 16.4 to 16.5, 16.15 to 16.16, 16.56a to c, and 19.32).

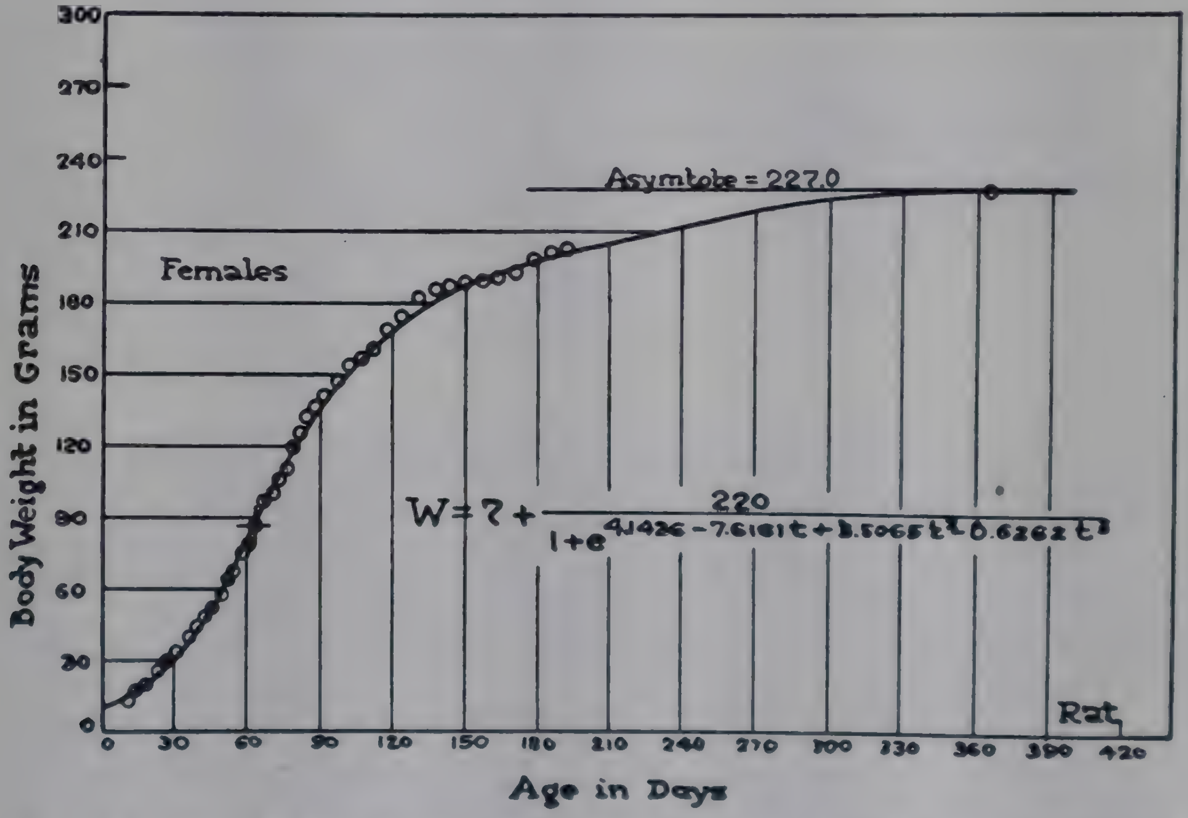

Fig. 16.58. The Verhulst-Pearl-Reed "logistic" growth equation. Compare to Fig. 16.4.

As we have seen, the time curve of growth—of individuals or populations—is composed of a segment of increasing slope and a segment of decreasing slope, with the inflection occurring at a critical period, flowering in plants, puberty in animals, and the end of a "free frontier" or some other critical era in population growth. Now Malthus' statement of the tendency of human population—in common with other populations—to increase exponentially, that is in a geometric progression, in this case doubling itself every 25 years, is correct for the period of unrestricted growth, for the segment of increasing slope.

This, indeed, is the history of the population growth in the United States between 1660 and 1880, as shown in Figs. 16.16 and 16.56. During these 220-odd years the population doubled itself every $23\frac{1}{2}$ years, quite close to Malthus' estimate of 25 years. The rate of this doubling is also shown by Curve 3, Fig. 56c; the doubling curve is quite horizontal, near 25 years between 1660 and 1880; the population increased at the rate of 2.96 per cent—about 3 per cent—per year.

Malthus, however, committed a common extrapolation error in saying that "in the next period, the population would be 56 million". The realization of the inherent tendency to grow, to increase in a geometric progression, at a constant percentage rate, occurs only when the environment does not restrict growth, a condition offered by the United States up until about 1880. Thereafter the expansive urge for geometric-progression increase is held in check by environmental limitations. Thus in the United States, closing of the frontiers, closing of the free-land era, shifting of the population from the farm (where wife and children are economic assets) to the city (where they are economic liabilities), increasing the period of education, increasing wants (automobile, radio and other gadgets) may all be considered as environmental limitations. Man is governed by man-made psychological factors—by fashions, if you please—even more than by intrinsic animal urges. Elsewhere, perhaps in India, China, and the Middle East, and so on, starvation and famines hold the population in check. Disease ravages may keep in

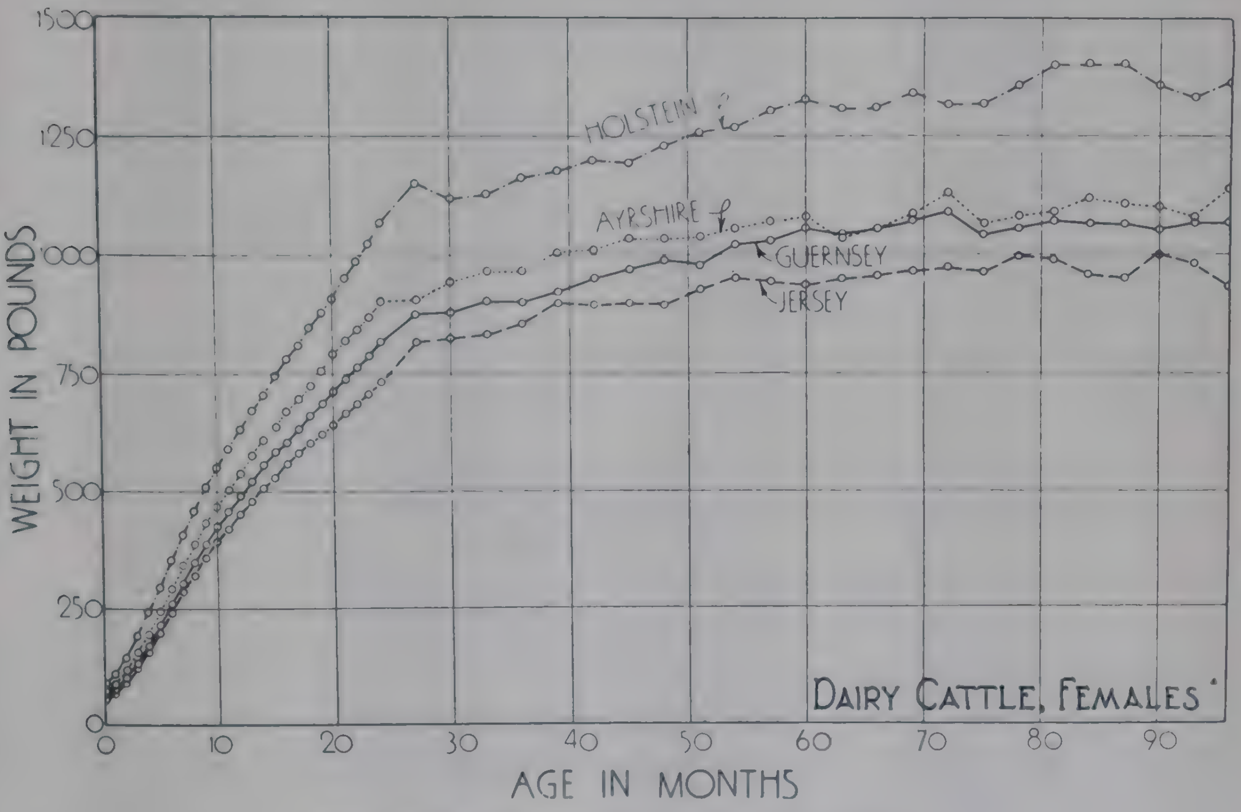

Fig. 16.59a. Growth in weight of cattle.

check overcrowded populations[41]. In the United States and other western-civilized countries, the limitation of the population is not usually caused by famine or plagues, but by more subtle factors, at least among the middle and upper classes sensitized to their operations. The "lower" classes are less attuned to the shifting of economic and psychologic winds and their reproductive pattern is more persistent, more stable[42]; but they suffer a higher infant mortality[43].

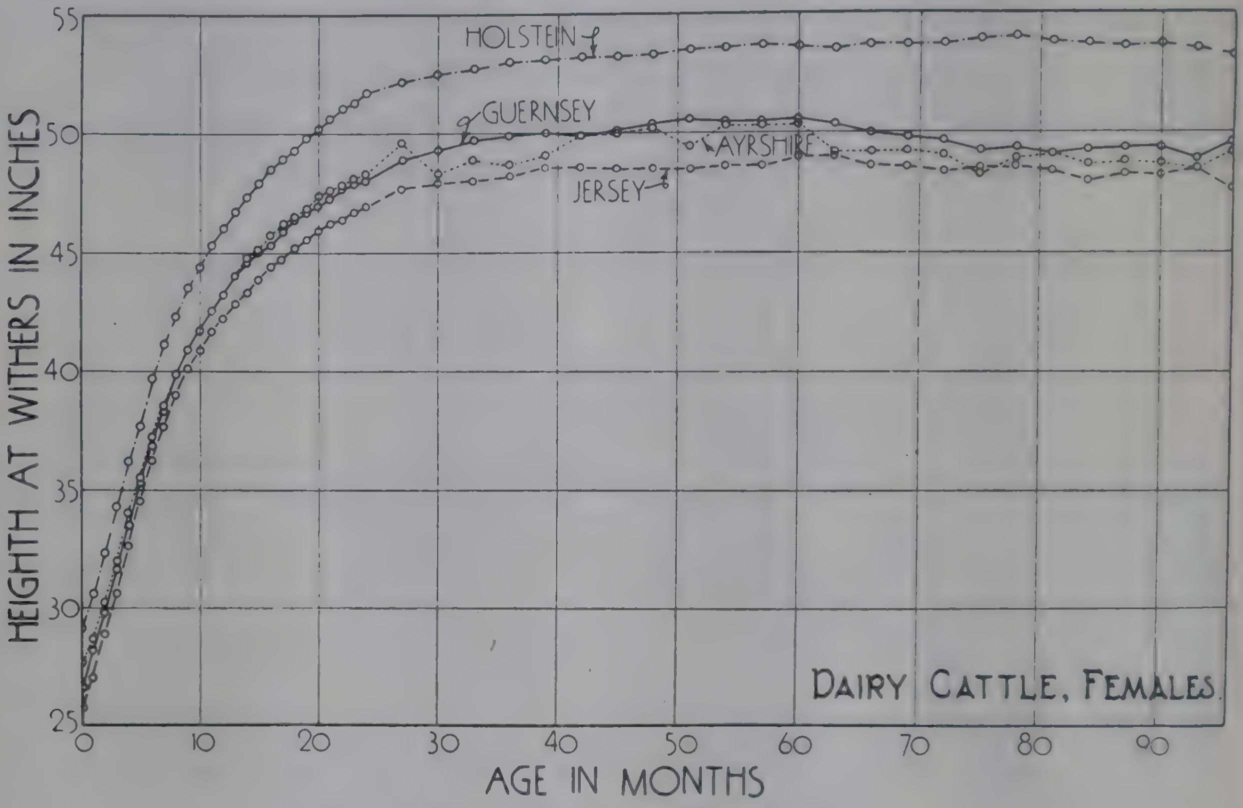

Fig. 16.59b. Growth in height of cattle.

The neuro-psychologic sensitiveness of our population to overcrowding recalls Pearl's observations[44] on the influence of overcrowding of flies, *Drosophila* in a half-pint bottle. All conditions were constantly favorable except the number of insects per bottle.

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[41] "Only one out of every five children born in Teheran lives to the age of six . . . The real public health problem, of course, is poverty."—W. L. Willkie, "One World," Simon and Schuster, 1943.

[42] For statistics on differential sex activity and child-bearing, see Pearl, R., "The biology of population growth," Knopf, 1925. "The natural history of population," Oxford University Press, 1939.

[43] Stopes, Marie, *J. Roy. Stat. Soc.*, **88**, 85 (1925): both pregnancy and child mortality increase with increasing poverty and ignorance.

[44] Pearl, R., *et. al.*, *J. Exp. Zool.*, **5**, 57 (1932); *Am. Naturalist*, **61**, 289 (1927). Also, Adolph, E. F., "The size of the body and the size of the environment in the growth of tadpoles." *Biol. Bull.*, **61**, 350 (1931); Bilski, F., "Lebensraumes und Wachstums," *Pflüger's Arch.*, **188**, 255 (1921); Goetsch, W., *Zool. Jahrb, Abt. allg. Zool. u. Physiol.*, **45**, 799 (1928), and others.

> The effect of density of population upon egg-laying was immediate. . . . The same flies were exposed to conditions of high density in alternating twenty-four hour periods. The rate of egg production per female per day was higher in the low-density periods than in the high. The view is developed . . . that crowding produces the observed effect on rate of egg laying primarily . . . as a result of a collision or interference action of the flies upon each other, which alters the normal physiologic equilibrium and processes of the individual, particularly with reference to three major functions—food intake, energy input in muscular activity, and oviposition.

We see here the operation of an elegantly delicate homeostatic mechanism for holding the population in check not involving the crude, cruel, ravages of starvation, disease, and attack of enemies, as we find under natural conditions.

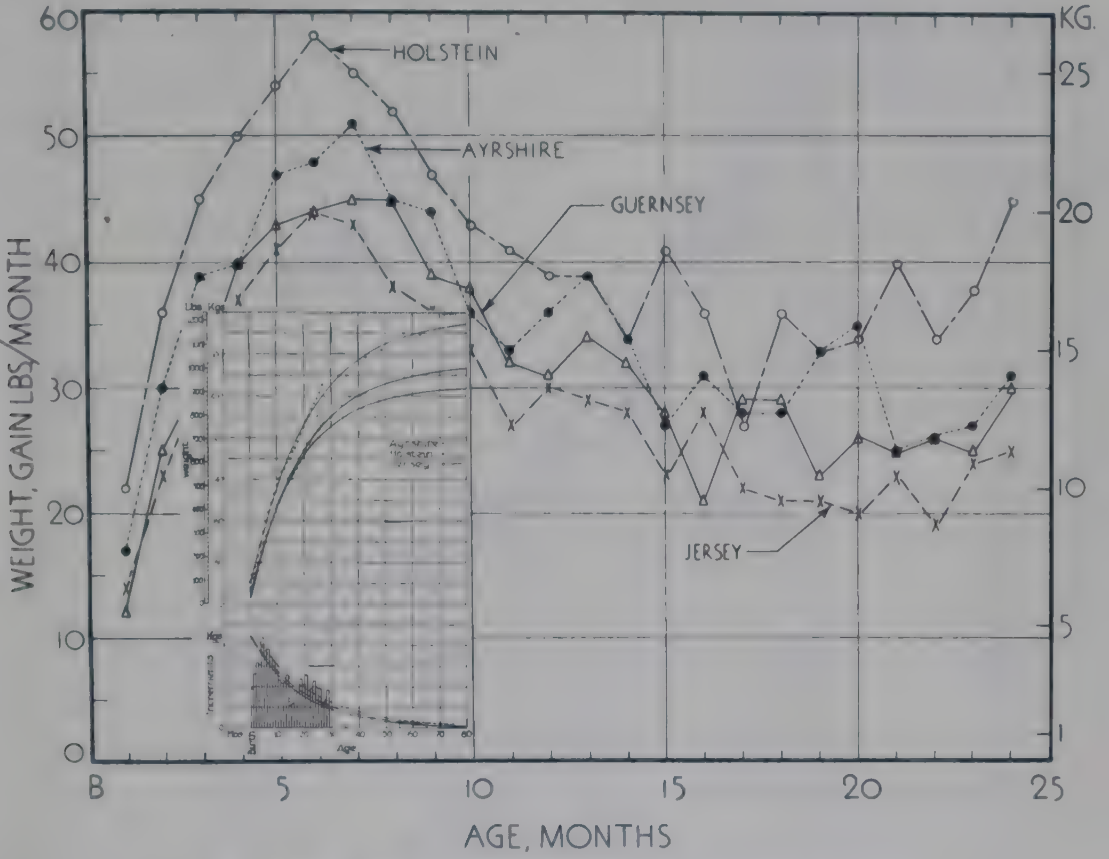

Fig. 16.59c. Weight increments in growing cattle.

It appears that the shape of the growth curve of Unites States population, especially of the more sensitive middle and upper classes (Fig. 16.56) is molded not by starvation, plagues, attacks of external enemies but by homeostatic mechanisms psychologic in nature, analogous in delicacy to that operating in the population of *Drosophila* confined in a half-pint bottle in the presence of abundant food, air, and absence of disease and natural enemies.

As previously noted, the situation is different in some human populations, especially in Asia; and even some highly civilized European peoples prefer (consciously or unconsciously) the overflow and war methods of homeostasis for keeping the population in check in accordance with the general law of sigmoid growth.

The overflow method of taking care of surplus population, of the urge to reproduce indefinitely in a geometric progression, is illustrated, on a small scale, in all its terrible drama in the periodic overflow of the lemming,[45] a species of field mouse. These animals breed in the upper altitudes of Norway, and every 3 to 4 years the population becomes too great for its normal habitat. So it overflows, and following the path of least resistance, migrates down the valley in search of food, finally reaching the sea where it drowns in countless thousands. Folk-lore has it that they migrate for ideological reasons, in search of a sunken Atlantic continent.

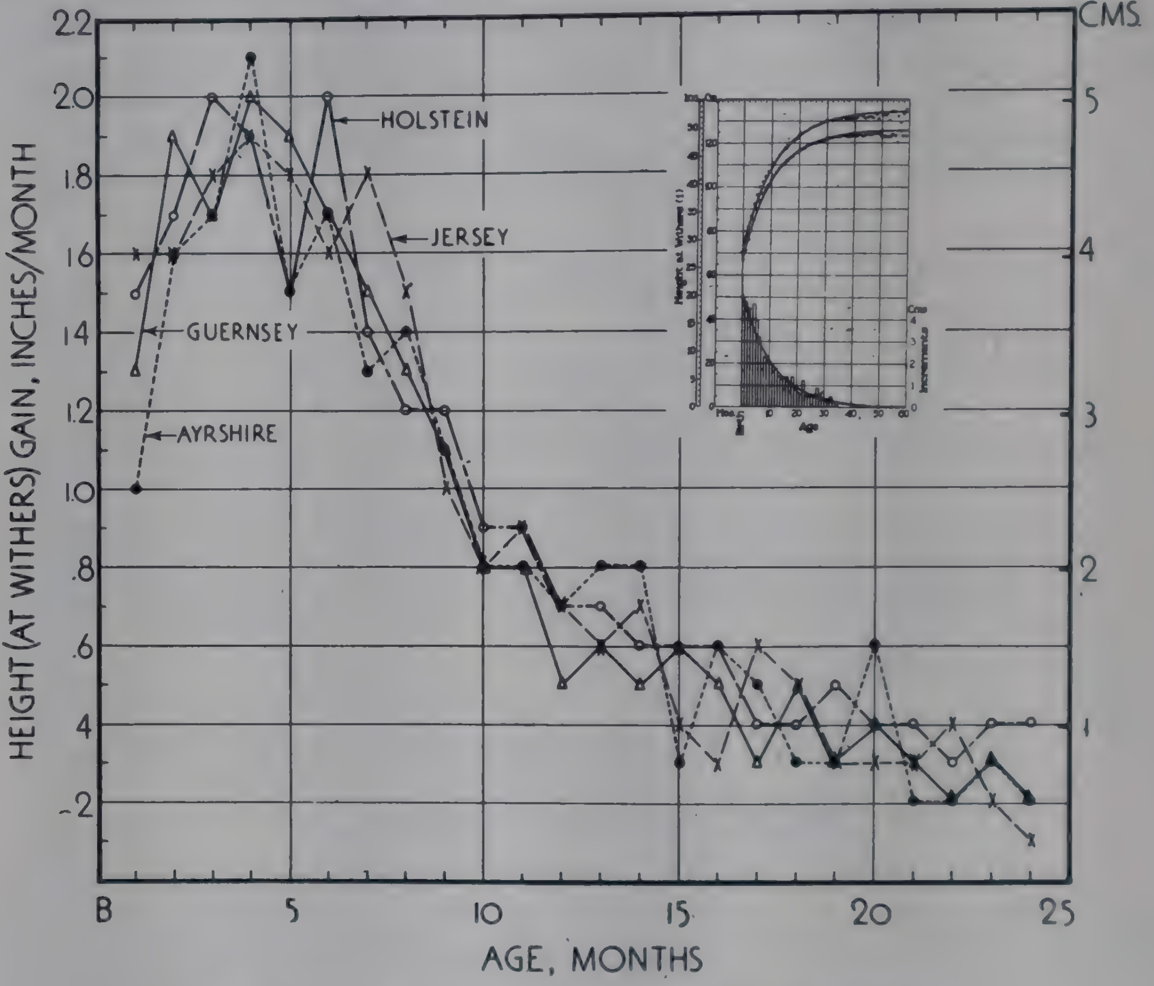

Fig. 16.59d. Height increments in growing cattle.

16.9: Comparison of our growth equations with some others. The age curve of growth in weight or in cell number when plotted on arithmetic paper consists of (1) a segment of increasing slope, a self-accelerating phase, reflecting predominantly the expansive drive to grow in geometric progression; (2) a segment of decreasing slope, a self-inhibiting phase, reflecting predominantly the back pressure of the environment on the expansive drive.

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[45] Elton, C. S., "Voles, Mice and Lemmings, Problems in Population Dynamics," Oxford, 1942.

During phase (1) the growth rate, dW/dt, tends to be proportional to the growth already made, to the weight, W, of the animal, as given by the equation

$$dW/dt = kW \tag{5}$$

This segment, however, shows several discontinuities or "breaks," analogous to metamorphosis.

During phase (2) the time rate of growth tends to be proportional to the available "living space," to the difference between the present weight, W, and the mature weight, A, as given by the relation

$$dW/dt = k(A - W) \tag{9}$$

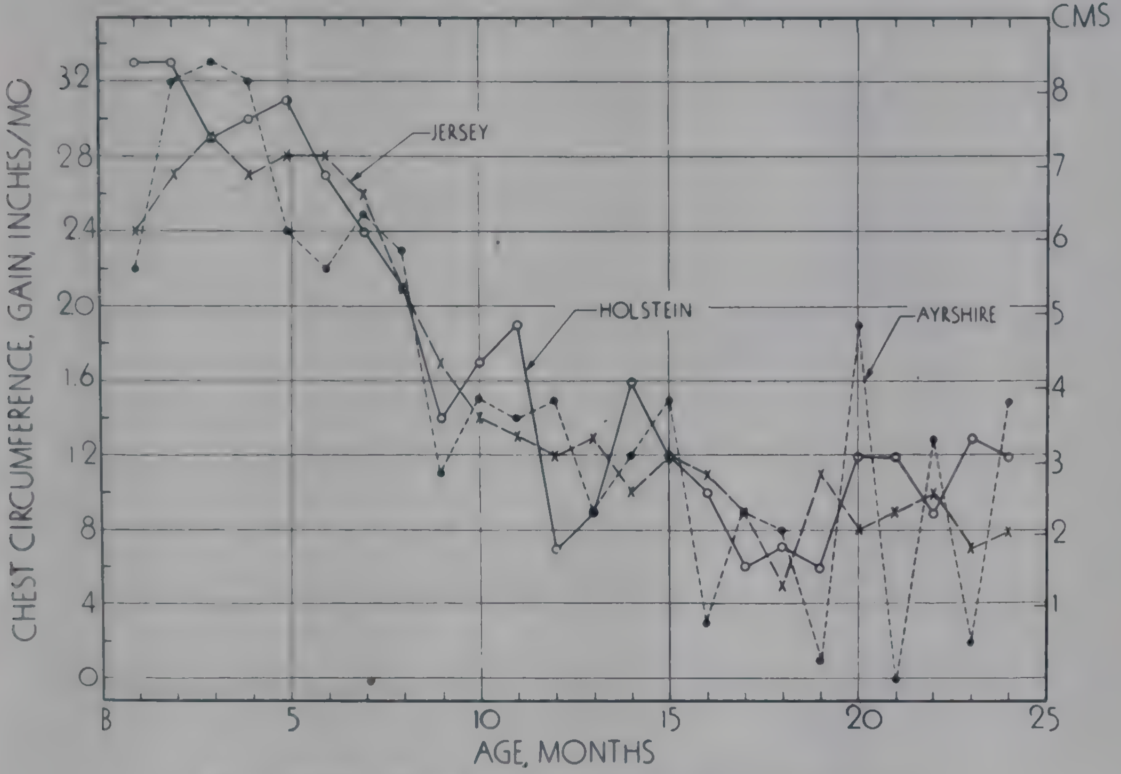

Fig. 16.59e. Chest increments in growing cattle.

On integrating the growth increments dW for the corresponding time intervals dt, the weight, W, of the animal is given as function of age, t. For equation (5) the integrated equation is

$$W = Ae^{kt} \tag{8}$$

and for equation (9),

$$W = A - Be^{-kt} \tag{12}$$

The numerical values of k have definite physical meanings: $100k$ is the percentage growth rate with respect to the growth already made (weight of the animal) in equations (5) and (8) and with respect to the growth yet to be made in equations (9) and (12). (Another physical definition of k: in equation (5), $dW/dt = k$ when $W = 1$; in equation (9), $dW/dt = k$ when $A - W = 1$.)

Special emphasis is placed on the fact that equations (5) and (9) do not represent growth rate as explicit functions of time, but of the condition of the growing system itself. Time is merely a frame of reference (Chs. 10 and 19) introduced as matter of convenience during the integration process.

Most other equations in the literature, on the contrary, represent growth rate as an explicit function of time. Thus the Pearl-Reed[46] logistic equation is

$$dW/dt = k_1t + k_2t^2 + k_3t^3 + \cdots).$$

Likewise the Glaser[47] equation is

$$dW/dt = k\,\frac{1}{2t+1}\,W, \quad \text{or} \quad \log W = k \log (2t + 1) + c$$

(The Glaser equation indicates that the percentage (or logarithmic) gain between, for example, the fifth and sixth day of growth of the chick embryo is proportional to $\frac{1}{6^2 - 5^2} = \frac{1}{11}$, and so on for each successive day; it is proportional to the difference between the squares of the final and initial age intervals. In equation form it may be written $\frac{dW}{dt} = \frac{K}{2}\frac{W}{t}$ or $\log W = \frac{K}{2} \log t$, or $\log W = k \log (2t + 1) + c$, in which $k = \frac{K}{2}$.)

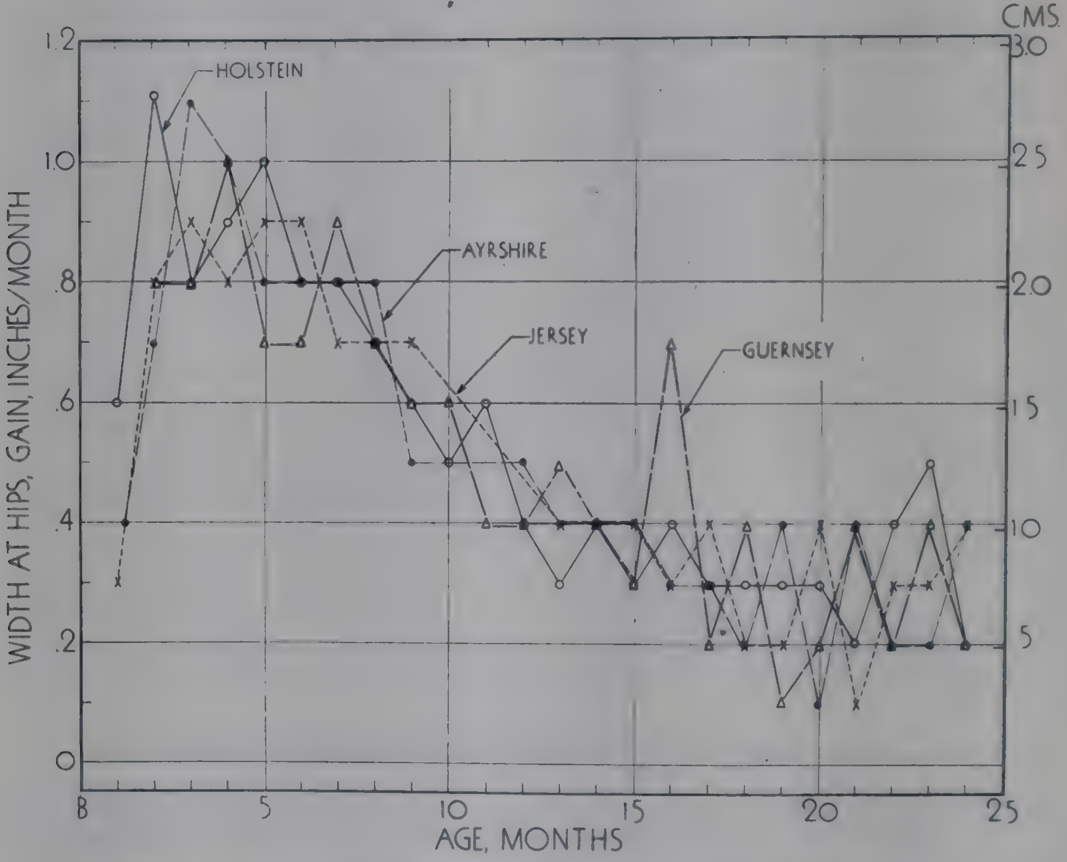

Fig. 16.59f. Increment of hip-width in growing cattle.

The MacDowell-Murray-Schmalhausen equation[48]

$$\log W = k \log (t - n) + c$$

is in principle identical with the Glaser equation.

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[46] Pearl, R., and Reed, L. J., *Metron*, **3,** 1 (1923), and many other papers.

[47] Glaser, O., *Biol. Rev.*, **13,** 20 (1938), and *Growth*, Supplement, p. 53 (1940).

[48] MacDowell, E. C. and C. G., Gates, W. H., and Allen, E., *J. Gen. Physiol.*, **11,** 57 (1927), and **13,** 529 (1930). Murray, H. A., Jr., *Id.*, **9,** 39 (1925). Schmalhausen, I., *Arch. Entwicklungsmech. Organ.*, **110,** 33 (1927), and **124,** 82 (1931).

These equations seem to be illogical because they are explicit functions of time rather than, as our equations (5) and (9), functions of the condition of the system itself.

It is natural to assume that time is an element of the growth process because growth is correlated with time. But it is well known that by appropriate experimental procedure, the growth process may be delayed or accelerated, whereas time, of course, continues to flow at a uniform rate. Thus, Osborne and Mendel succeeded in arresting the growth process in the albino rat from the age of about 2 to 17 months; then when the animals were placed on an adequate diet, growth was resumed at a rate which was characteristic of the species *for the given weight*, and *not for the given age*. This statement is substantiated by the excellent fit of equation (9) or (12) to the data of Osborne and Mendel as shown in Fig. 19.16.

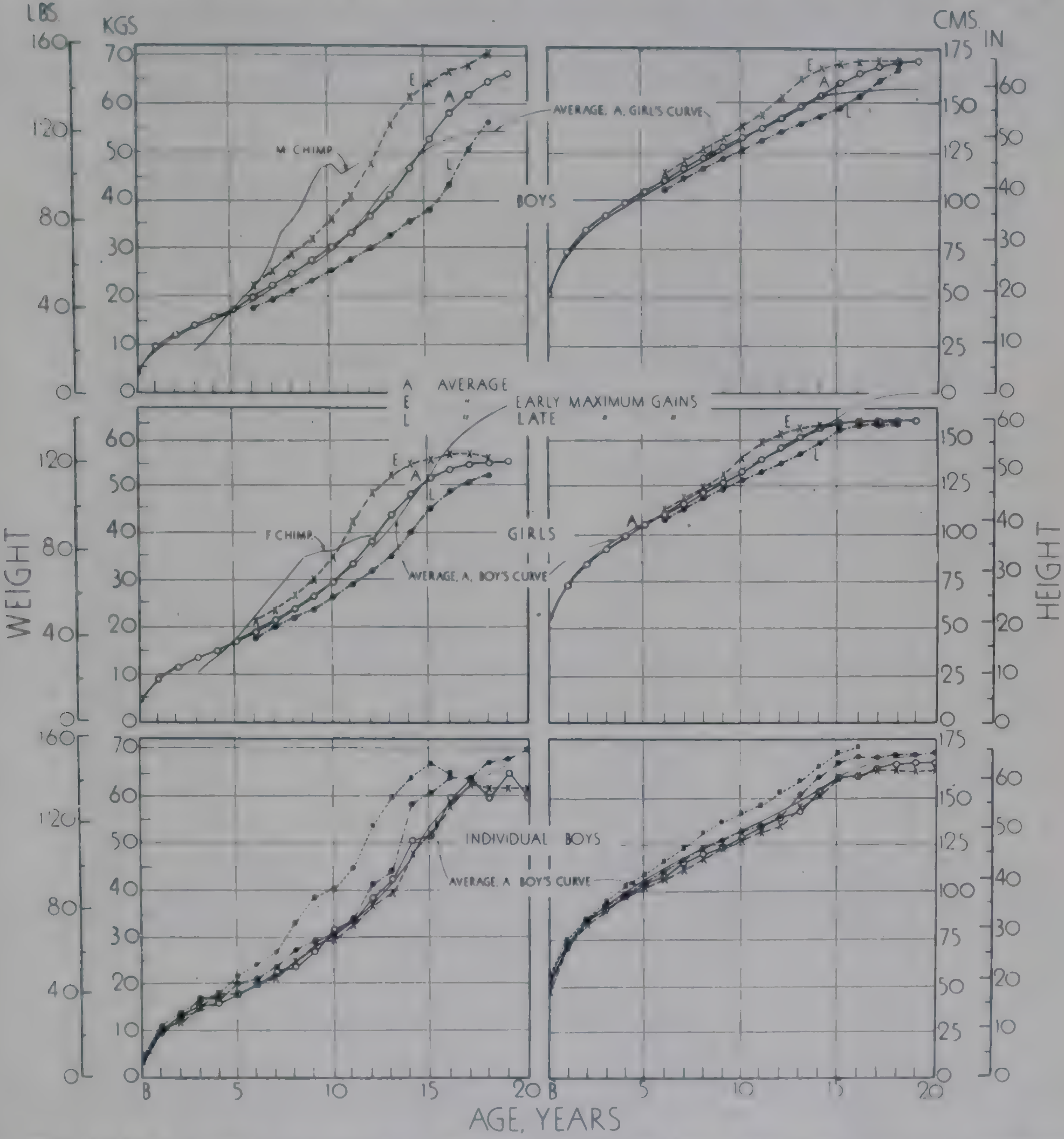

Fig. 16.60a. Growth of children, average, early and late maturing, plotted from several sources: averages by Shuttleworth and by Baldwin, *l.c.*; the curves for the *same* individuals (boys) from birth to 20 years by Max Guttmann, *Z. Kinderheilkunde*, **13,** 248 (1916); the curves of chimpanzees (male, M, and female, F) by K. W. Spence and R. M. Yerkes, *Am. J. Phys. Anthrop.*, **22,** 229 (1937). A = average; E = early maturing; L = late maturing.

The above MacDowell-Murray-Schmalhausen equation shows that the logarithms (or percentages) of size vary directly with the logarithms (or percentages) of time. It is logical to assume that the number of cells increases logarithmically, that is, in geometric progression; but it does not seem logical to assume that time flows logarithmically.

We have been criticized for assuming the presence of discontinuities, "breaks," in the age curve of growth during the self-accelerating phase. But the critics' equations likewise represent only limited segments of the curve. The presence of discontinuities in the growth curve was also substantiated directly by Lerner,[49] Romanoff,[50] and others.

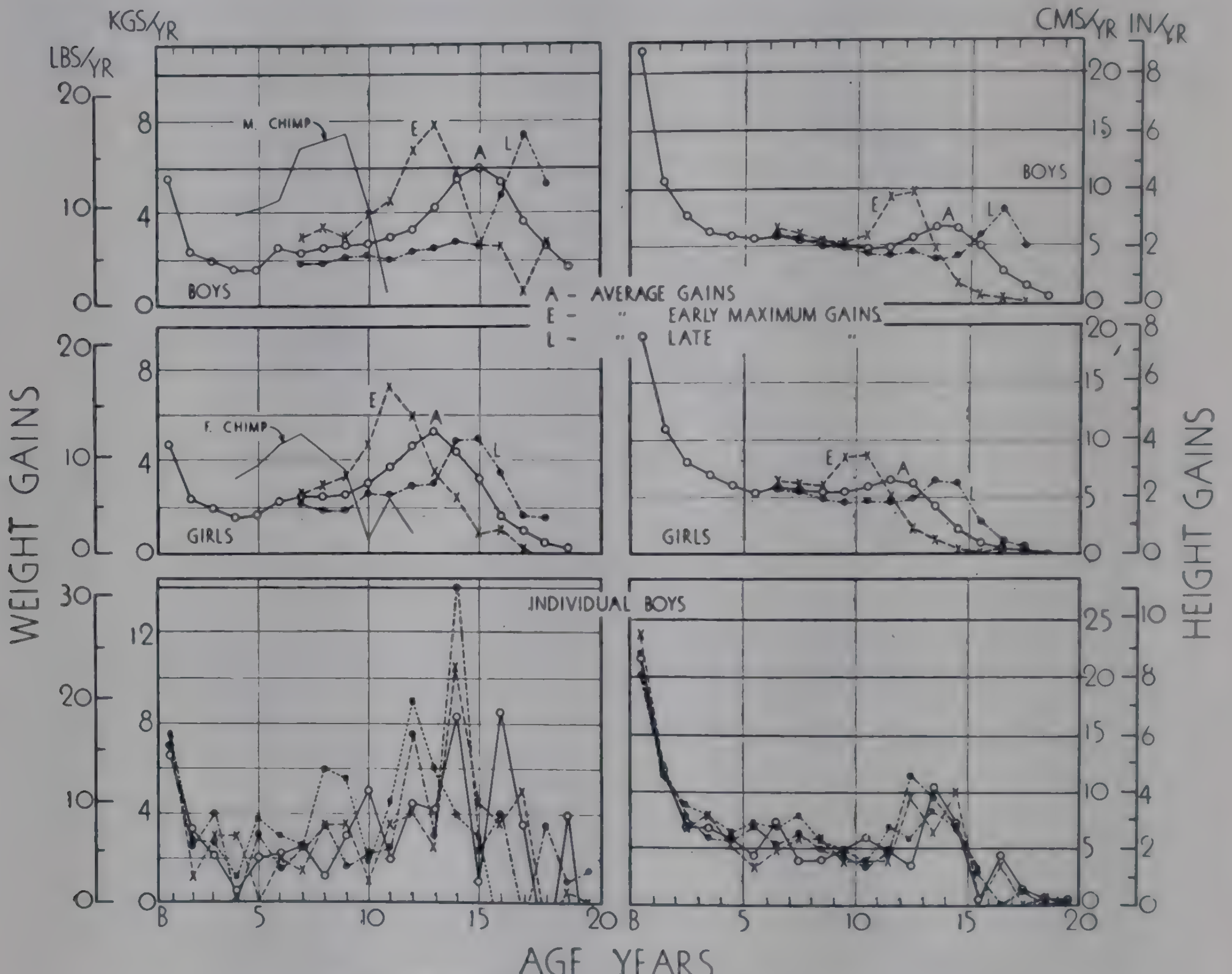

Fig. 16.60b. See legend for Fig. 16.60a

It is illogical to object to the presence of relative discontinuities in the growth curve when their presence in the individual (metamorphoses, most conspicuously in cold-blooded animals) and in the race (emergent evolution) are generally known. When external conditions are equal, growth exhibits general statistical continuity in its path toward a certain equilibrium, but within this *general* continuity there appear to be *detailed* discontinuities.

The use of equations for representing growth has been criticized because they do not give insight into the detailed growth mechanisms. Neither does the law of gravitation explain detailed mechanisms of gravitation; it only claims rational meaning for its constants. The equations we employed represent regularities, namely that the growth rate tends to be directly proportional to the number of reproducing cells or to the available "living space" and the equation constants have definite, rational, physical meaning. If the value of k in our equation is constant, it means, by definition, regardless of theory, that the percentage growth rate is constant during a given time interval. If the value of k changes, the percentage rate of growth changes. The use of this equation to describe data is intended to assist and to guide, not to replace experimental analysis, as has been mistakenly suggested. Experimental and mathematical analyses, like other action and thought, are mutually supplementary.

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[49] Lerner, I. M., *Science*, **89**, 16 (1939).

[50] Romanoff, A. L., *Science*, **70**, 484 (1929).

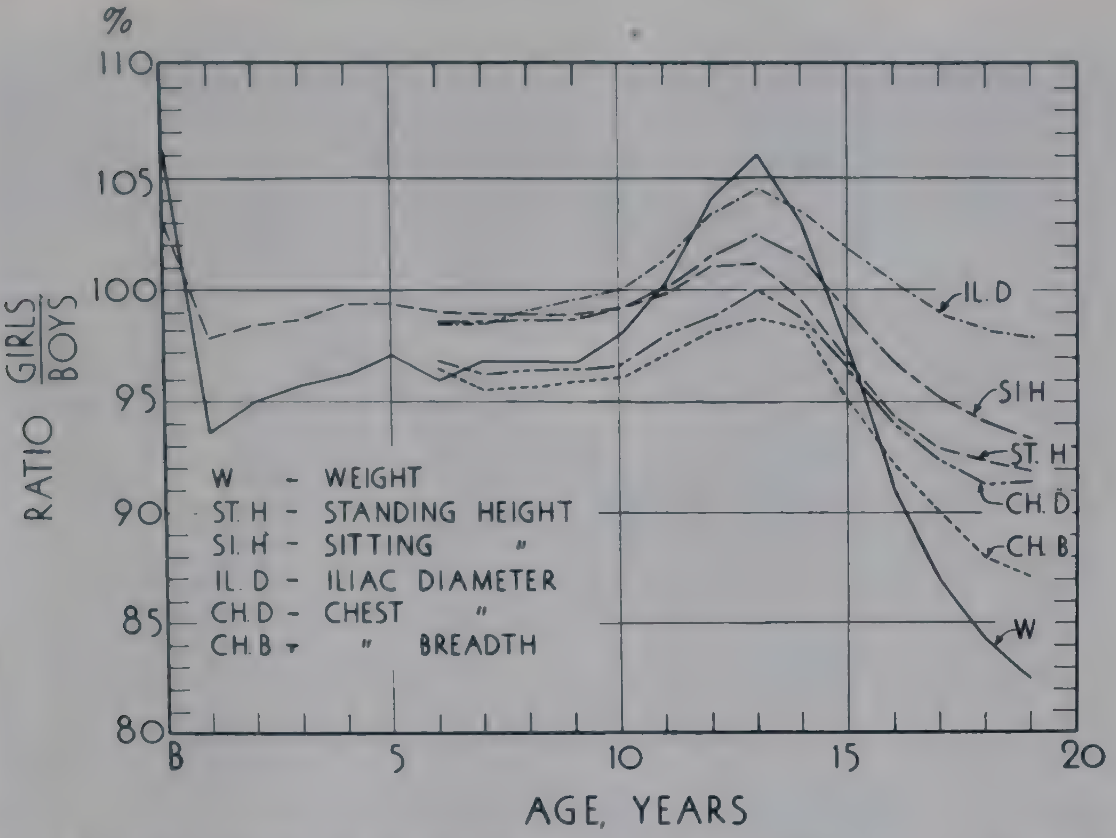

Fig. 16.61. Age changes in the ratios of size of girls to boys. At birth and at age 13 years girls are about 6 per cent heavier than boys; on approach to maturity the boys overreach the girls to the extent of about 20 per cent for weight and 8 per cent for height. (See Chapter 7 for endocrinological mechanisms.)

On the basis of physico-chemical considerations of the growth process, Robertson[51] inferred that growth is an autocatalytic process and that the velocity of growth may be limited by a monomolecular autocatalytic chemical reaction, given by the equation

$$dW/dt = kW(A - W)$$

indicating that the velocity of growth is a function of both growth already made and growth yet to be made.

This equation represents a symmetrical curve, while growth curves are not usually symmetrical; that is, the inflection does not occur in the center of the curve (Figs. 16.57a and b). Attempts to rationalize this[51, 52] lead to practical difficulties. For this reason we broke up the curve into its components and represented them by the equations $dW/dt = k_1W$ and $dW/dt = k_2(A - W)$, which proved successful in our hands as indicated by the many curves in this chapter.

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[51] Robertson, T. B., "Chemical basis of growth and senescence," Lippincott, 1923.
[52] Crozier, W. J., *J. Gen. Physiol.*, **10**, 53 (1926).

To overcome the difficulty of asymmetry in Robertson's equation, Pearl and Reed[53] converted it to a potential series function of time, t, given by the relation

$$\frac{dW/dt}{W(A - W)} = k_1 t + k_2 t^2 + k_3 t^3 + \cdots + k_n t^n.$$

Pearl and Reed were concerned with the integrated form of this equation, namely

$$W = d + \frac{A}{1 + me^{k_1 t + k_2 t^2 + k_3 t^3 + \cdots + k_n t^n}}$$

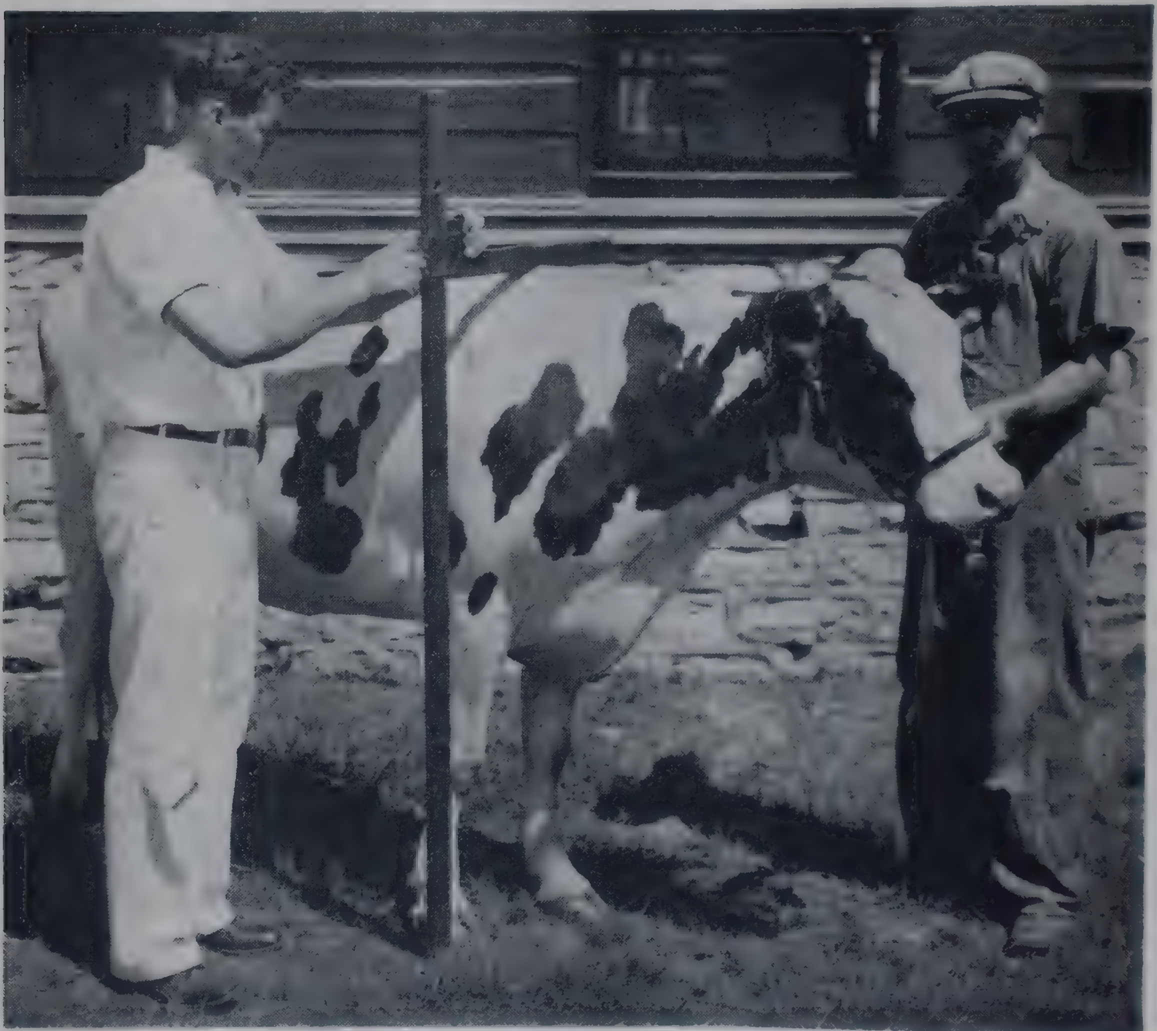

Fig. 16.62a. Measuring the height of withers at the highest point. The horizontal arm and vertical arm of the measuring device are equipped with built-in spirit levels to help keep the measuring rod in strictly vertical position.

They found it elastic enough to fit the growth curve of the rat, but only beginning with 10 days after birth, as shown in Fig. 16.58. It does not represent the curve from conception to 10 days following birth, the most important developmental stages in the life history. The numerical values of the constants, k, k_1, k_2 $\cdots$ change with the number of constants employed. Hence, one cannot give definite, numerical meaning to the constant, and it is therefore, from our special viewpoint, irrational.

Another well-known growth equation is that of Gompertz[54]

$$W = Ae^{-e^{-t}}$$

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[53] Pearl and Reed,[46] and many other papers.

[54] Gompertz, S., *Phil. Trans. Roy. Soc.*, p. 522 (1825).

in which W is the size of the organism or population at time t, A is maximum size, and e is the base of natural logarithms. It is also written as $W = Ae^{ce^{kt}}$

Its many constants make it a potential series, and it is therefore meaningless from our viewpoint. It states that for a given growth cycle the log-logs of the percentage of growth increase directly with time. Courtis[55] employs this equation widely for growth.

Many other equations have been proposed which we have not discussed, partly because they fail to meet the criterion of definiteness and rationality of meaning of the constants (Sect. 10.10).

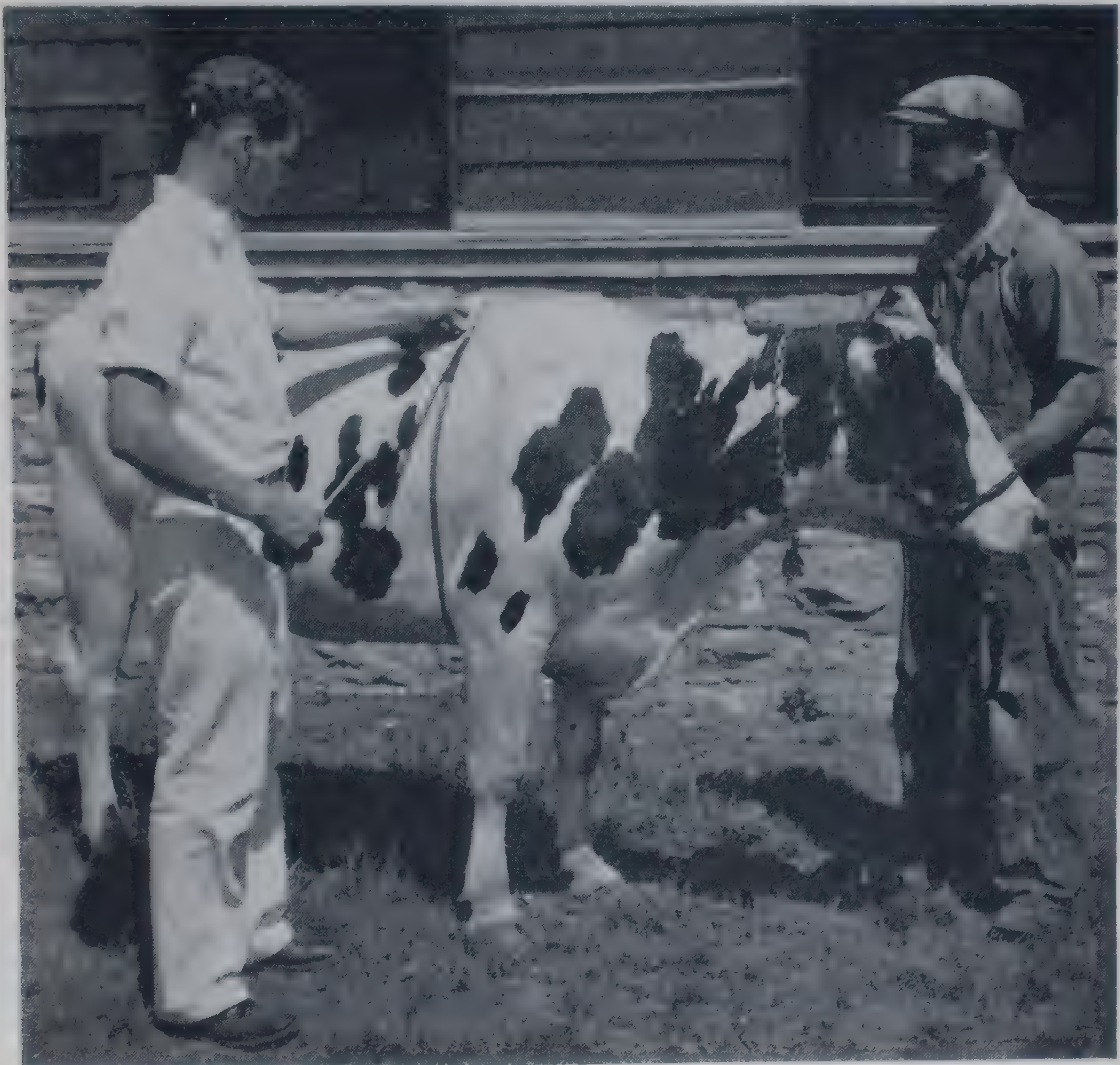

Fig. 16.62b. Measuring heart girth.

In summary, it does not appear possible to represent the entire growth curve by one equation, not even by the very plastic potential series equations. In other words, growth curves appear to have metamorphosis-like discontinuities[56, 57].

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[55] Courtis, S. A., *Growth*, **1**, 155 (1937).

[56] Davenport, C. B., "Human metamorphosis," *Am. J. Physical Anthropol.*, **9**, 205 (1926), and *J. Gen. Physiol.*, **10**, 205 (1926).

[57] Knibbs, J. H., *J. Am. Stat. Assn.*, **21**, 381 (1926), and **22**, 49 (1927), reported that the time curve of human populations show breaks. For other critical discussions of growth equations, see Yule, G. V., *J. Roy. Stat. Soc.*, **88**, 1 (1925); Crozier, W. J., *J. Gen. Physiol.*, **10**, 53 (1926); Gray, J., *Brit. J. Exp. Biol.*, **6**, 248 (1928-29); Wilson, E. B., and Puffer, R. R., *Am. Ac. Arts and Sci.*, **68**, 285 (1933).

Wetzel[58] published an elaborate, perhaps rational, analysis of growth as a "mode of motion." Unfortunately, the writer is not able to follow his detailed analyses.

16.10: Summary. Growth is self-multiplication of reproducing units, either of individuals in a population or of cells in a multicellular organism. Growth curves of populations and of multicellular organisms are remarkably similar.

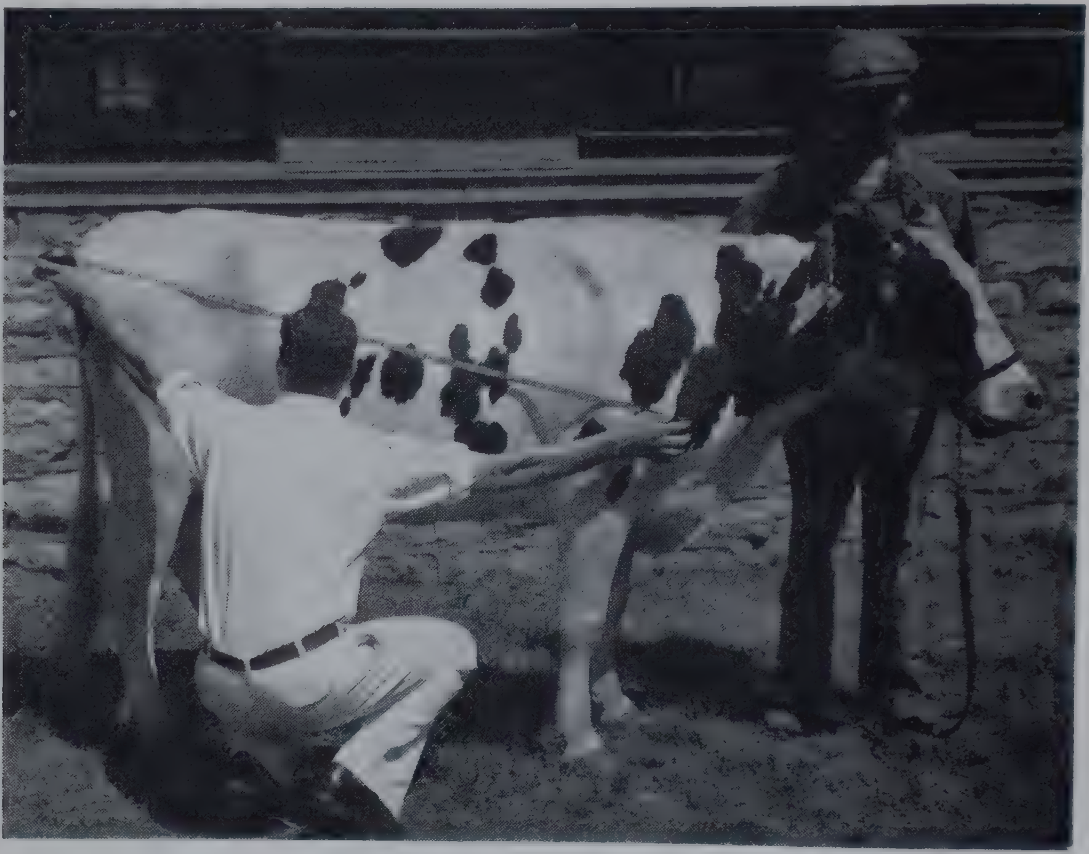

Fig. 16.62c. Measuring the distance from a point of shoulders to ischium.

Broadly speaking, the growth curve is molded by two factors: (1) an expansive drive tending toward expansion of self or kind, to multiply indefinitely, and (2) an environmental pressure which keeps the expansive urge under control.

Early in the history of the individual or population when growth is unrestricted by the environment, the *percentage* growth rate tends to remain constant as represented by the rate equation, $dW/dt = kW$, or by the cumulative equation, $W = Ae^{kt}$. The proportionality constant, k, is the relative, or when multiplied by 100, the *percentage* growth rate of the population or individual under the given conditions, computed on the differential or instantaneous-rate basis.

The *instantaneous* percentage rate, $100k$, of growth in the earliest, unrestricted, phase of growth is in the chick during the first 5 days about 100 per cent *per day* (doubled in 17 hours), and probably also in the rabbit, mouse, rat, monkey, and guinea pig. The instantaneous rate of growth of a pumpkin under field conditions was 40 per cent *per week* (doubled in weight in 1.7 weeks); of a wheat plant, 74 per cent *per week* (doubled in 0.94 week); of a barley plant, 60 per cent *per week* (doubled in weight in 1.2 weeks).

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[58] Wetzel, N. C., *Growth*, 1, 6 (1937), and many other papers.

During the unrestricted phase of *population growth* the instantaneous percentage growth rate was 185 per cent per hour (doubling in 0.37 hour) for *B. coli* at 37° C; 47 per cent per hour (doubling in 1.5 hours) for lactic-acid accumulation in milk by *B. l. a.* at 25° C: 2.9 per cent per year (doubled in 24 years) for the growth of the human population in the United States during 1660–1860, and so on.

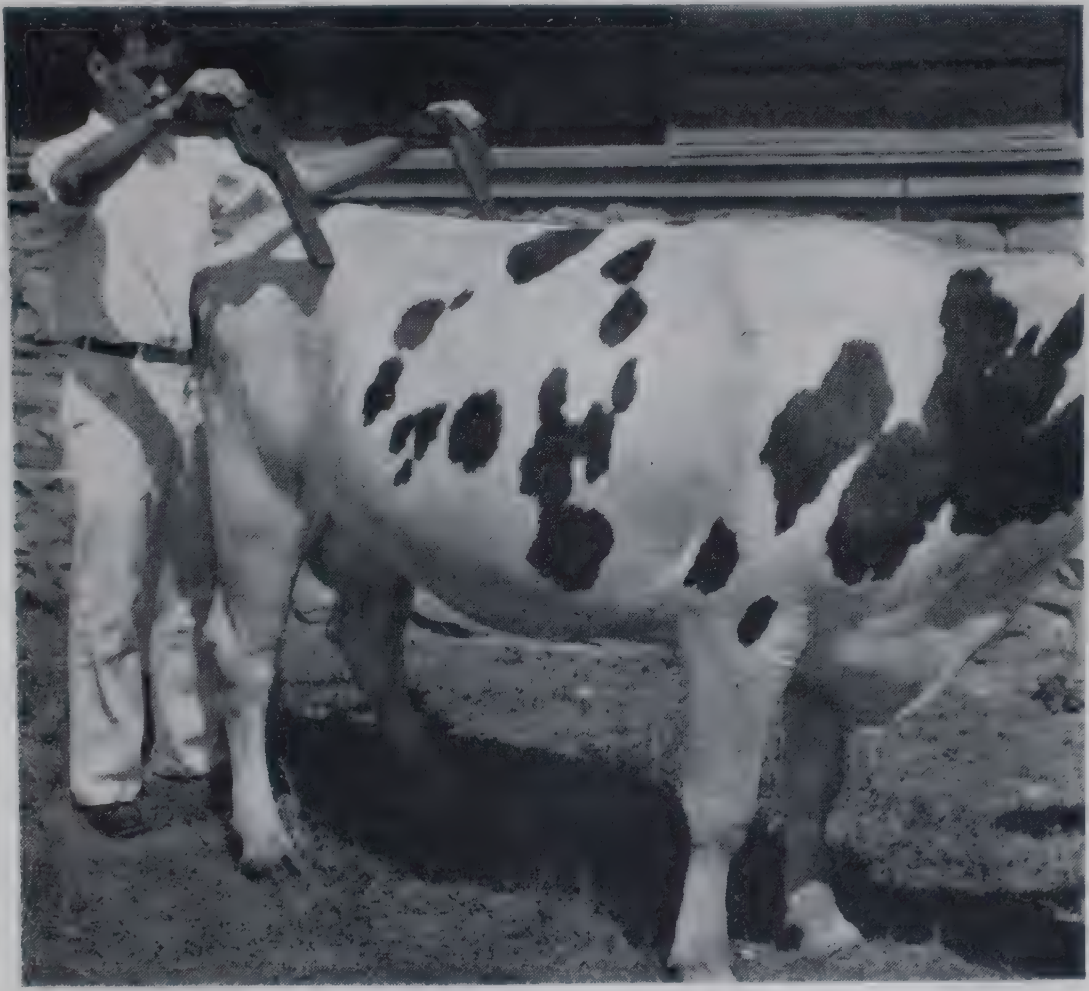

Fig. 16.62d. Measuring the width of hips.

After the individual or the population attains a certain size, the environmental limitation retards the intrinisic growth rate and the slope of the growth curve is reversed from increasing to decreasing. This slope reversal coincides with puberty in animals, flowering in plants, and with a tendency to overcrowding in populations. While there is great diversity in the *detailed* mechanisms actuating the reversal in the shape of the curve, the *general* feature—shape of the curve—is the same whether the growth is populations of men or flies trapped in an isolated space, or cells trapped in the body of a multicellular organism. Environmental limitations finally bring the growth process to a standstill, although the maintenance aspect of growth continues for some time in individuals and may continue indefinitely in populations. Cessation of growth in *individual* organisms always leads to senescence and death (Ch. 18). A similar fate of senescence and death overtakes *some* populations in some environments, such as of yeast in fermenting juice or lactic-acid organisms in milk. Populations which are members of broader cycles, such as mice or men, are apparently able, in the absence of some catastrophe, to reproduce and thus "keep the population young" indefinitely (at least in theory).

The rate of growth following the permanent reversal or major inflection in the slope of the age curve is no longer proportional to the existing size, W, of the population or organism, but to the available "living space", reflected by the growth yet to be made, represented symbolically by $A - W$, in which A is the mature or maximum value of the population or of the individual. The instantaneous growth rate during this period is consequently represented by the rate equation $dW/dt = k(A - W)$; or the total population or organism size at age t is given by the integral equation $W = A - Be^{kt}$. The proportionality constant k is the relative or, when multiplied by 100, percentage growth rate in respect to growth yet to be made to reach the mature size A, as contrasted to the k for the early, unrestricted, phase of growth which represents the relative growth rate with respect to growth already made, to the size, W, of the reproducing population or organism.

The numerical value of k for the phase of growth following the major inflection in the curve tends to vary with the mature size of the population or organism. It is 0.04 to 0.05 (that is, 4 to 5 per cent) *per month* in cattle (80 to 100 months required to reach 98 per cent mature weight); 0.35 to 0.70 *per month* in rats (6 to 12 months required to reach 98 per cent mature weight); 0.62 to 0.80 *per month* in mice (5 to 7 months to reach 98 per cent mature weight); 0.80 to 1.6 *per month* in pigeons (3 to 7 months to reach 98 per cent mature weight); 0.025 *per year* in humans (18 to 25 years to reach 98 per cent mature weight); 0.47 *per day* in a yeast *population*; 0.08 *per day* in an oat plant; 0.26 *per day* in a squash plant, and so on (Table 16.1).

It is evident that the mass-action principle may be applied to both early (self-accelerating) and late (self-inhibiting) phases of growth. In early growth the rate of growth tends to be proportional to the growth already made, W, and in late growth to the growth yet to be made $(A - W)$.

The principle of mass action is applicable to many non-biologic types of growth, such as to the rate of increase of an inorganic product in a chemical reaction. Indeed, the principle of mass action was originally formulated by Berthollet (1799) and substantiated experimentally by Wilhelmy (1850) for chemical reactions *in vitro*, and, independently, by economists for economic processes in the form of the law of diminishing returns (Ch. 5). The expansion of many economic enterprises tends to follow a course similar to growth with early, apparently unlimited (self-accelerating) prosperity, gradually shifting into an era of diminishing returns. The mechanisms in these various processes are, of course, very different in detail but very similar in general plan (Ch. 5). The inherent limitation of the universe controls any type of indefinite expansion.

The equations of the two segments of the time curve of growth, as for chemical reactions, may be combined into one equation, $dW/dt = kW(A - W)$, which represents the rate of the autocatalytic monomolecular reaction of the physical chemist, widely used with slight modifications by Robertson and Wolfgang Ostwald, which attracted much attention and exerted great influence on the growth literature. Many modifications of this equation have been used by adding constants, thus turning it into a potential series, plastic but less meaningful. No equation has been found to represent *the whole* of the growth cycle of animals, although the Robertson-Ostwald and the Verhulst-Pearl-Reed equations were meant to be such. The actual growth curve shows breaks, illustrated most dramatically by metamorphosis in cold-blooded animals (from tadpole to frog, from larval to fly stage), birth, hatching and puberty in warm-blood animals, and change from aquatic to terrestial modes of respiration in birds (chicks during the 18th day of incubation). There appear to be similar irregularities in the growth of populations. For this reason, we prefer to break up the age curve, as far as possible, into its significant constitutent segments and employ separate equations with rational, clearly defined, constants to represent each segment.

Discussions are presented on genetic growth constants, together with numerical values of mature size of different species of animals, and times required to reach different fractions of the mature weight; on the relation between average and individual growth curves; and on some common factors influencing growth rates.

These equations are used in Chapter 19 for evaluating growth equivalence.

16.11: Appendix. This section contains several sets of numerical growth data, some genetic growth constants, and several charts which could not be included in the text.

Growth of dairy cattle. These data are based on Missouri Station Bulletin 336, 1934, by Ragsdale, *et al.*, and are also presented graphically in terms of weight and height as functions of age, and also in terms of gains per month (Figs. 16.59a to f).

We published a great deal of data, with their sources, on growth of various laboratory and farm animals in Missouri Res. Bul. 96. It would take too much space to reproduce them in this book, but most of them are represented in graphic form in the text of this chapter. Moreover, readers not familiar with the various classes of laboratory and farm animals will not appreciate the significance of the numerical data. However, everyone appreciates the significance of weights and heights of children; so the most recent data [59, 60] on growth of children are here presented, both for the average of all children measured (average of about 700 for each age) and for "early maturing" and "late maturing" (those having the "prepubertural acceleration" early and late).

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[59] Shuttleworth, F. K., "The physical and mental growth of girls and boys age six to nineteen in relation to age at maximum growth," Monographs of the Society for Research in Child Development, Vol. 4, no. 3, Serial 22, 1939, National Research Council, Washington, D. C. For ages 1, 2, 3, 4, and 5 years, the data are after R. M. Woodbury, U.S.D. Labor, Children's Bureau, Pub. 87, 1921.

[60] For the compilation of most available data on growth of children, see Baldwin, B. T., "The physical growth of children from birth to maturity," *Univ. Iowa Studies in Child Welfare,* **1,** no. 1 (1921).

Growth of Children

Age years	Weight				Height				Weight (kg) comparisons of early and late maturing*				Height (cm) comparisons of early and late maturing*			
	Boys		Girls		Boys		Girls		Boys		Girls		Boys		Girls	
	Kg.	Lb.	Kg.	Lb.	Cm.	In.	Cm.	In.	Early	Late	Early	Late	Early	Late	Early	Late
1	9.6	21.2	9.0	19.9	74.6	29.4	73.0	28.7								
2	12.0	26.5	11.4	25.2	85.4	33.6	84.0	33.1								
3	14.0	30.8	13.4	29.6	93.2	36.7	92.0	36.2								
4	15.6	34.4	15.0	33.1	99.6	39.2	99.0	39.0								
5	17.2	37.9	16.7	36.8	105.7	41.6	105.0	41.3								
6	19.8	43.6	19.0	42.0	111.5	43.9	110.4	43.5	22.4	17.4	21.2	17.8	115.6	106.7	112.7	107.6
7	22.2	49.0	21.5	47.4	117.6	46.3	116.3	45.8	25.5	19.3	23.8	20.0	122.3	112.5	119.2	113.3
8	24.8	54.8	24.0	52.9	123.3	48.5	122.0	48.0	29.0	21.2	26.8	21.9	128.5	117.9	125.4	118.8
9	27.5	60.7	26.6	58.8	128.8	50.7	127.4	50.2	32.1	23.4	30.2	23.8	134.2	123.0	131.5	123.6
10	30.3	66.8	29.7	65.4	133.9	52.7	132.8	52.3	36.2	25.7	35.0	26.5	139.7	128.1	140.0	128.1
11	33.4	73.6	33.5	73.9	138.8	54.6	138.7	54.6	40.9	27.8	42.4	29.1	145.8	132.5	148.6	132.7
12	36.8	81.2	38.3	84.5	143.8	56.6	145.2	57.2	47.8	30.3	48.5	32.1	155.2	136.8	153.7	137.2
13	41.2	90.9	43.7	96.3	149.6	58.9	151.4	59.6	55.8	32.9	52.1	35.2	164.9	141.4	156.0	142.0
14	46.8	103.1	48.2	106.4	156.4	61.6	155.6	61.2	61.8	35.8	54.6	40.2	169.8	145.3	157.3	148.4
15	52.9	116.7	51.5	113.6	163.1	64.2	157.8	62.1	64.6	38.5	55.5	45.3	171.7	149.5	157.7	154.6
16	58.4	128.6	53.2	117.4	168.3	66.3	158.8	62.5	67.3	43.4	56.6	48.9	172.5	155.6	157.8	157.5
17	62.2	137.1	54.2	119.5	171.3	67.5	159.3	62.7	68.0	51.0	56.9	50.6	173.1	163.9	158.1	158.7
18	64.9	143.1	54.7	120.7	173.0	68.1	159.6	62.8	70.9	56.4	56.0	52.2	173.3	169.0	158.4	159.2
19	66.7	146.9	55.0	121.3	173.8	68.4	159.6	62.9								

* "Early and late maturing" refers, respectively, to early and late maximal gain, MG. For boys early MG was observed at 12 years, late MG at 17 years; for girls early MG was observed at 10.5 years, late MG at 14.5 years.

TABLE 16.1. GENETIC GROWTH CONSTANTS

Animal	A (Mature Wt.)		B	$100k$[1] (Percentage of monthly decline)	t^*	Age[2] (from conception) at		
						50% mature weight	75% mature weight	98% mature weight
	(*kg.*)	(*lb.*)	(*kg.*)		(*mos*).	(*mos.*)	(*mos.*)	(*mos.*)
Beef cattle								
(Moulton *et al.*, Missouri data). Hereford-Shorthorn, castrated males	1100	2425	1600	3.47	10.7	31	51	124
Dairy cattle								
(Eckles *et al.*, Missouri) Holstein-Friesian, females	550	1215	805	4.6	8.3	23	39	93
Ayrshire, females	460	1014	725	5.0	9.1	23	37	87
Jersey, females	420	926	680	5.4	8.9	22	35	81
Dairy cattle								
Register of Merit Jersey Cattle, females, Missouri compilation	436	961	441	5.0	0.2	14	28	78
Horses								
Trowbridge and Chittenden (Missouri data)								
Percheron, females	678	1493	1677	8.2	11.0	19.5	28.0	58.7
Males, castrated	636	1400	1501	7.8	11.0	19.9	28.8	61.2
Swine								
(Mumford *et al.*, Missouri) Duroc-Jersey, females (early breeding data)	200	441	260	6.2	4.4	15.0	26.0	67.0
Sheep								
Hampshire, males (Trowbridge *et al.*, Missouri)	90	198	170	13.6	4.7	9.8	15.0	33.2
Suffolk females (Murray)	80	176	200	18.5	5.0	8.7	12.5	26.0
Shropshire x Merino, females (Murray)	50	110	120	18.8	4.7	8.3	12.2	25.3
Rabbit								
(Minot)								
Females	3.9	6.5	4.6	15.3	1.1	5.6	10.1	26.6
Males	3.0	6.5	3.9	25.3	1.0	3.9	6.6	16.6
Males and females (Castle)	3.2	7.1	8.0	43.4	2.7	3.7	5.3	11.1
Flemish								
Fl Himalayan x Flemish	2.8	6.2	9.2	44.7	2.2	4.2	5.8	11.4
Fl Polish x Flemish	2.5	5.5	11.0	49.2	3.0	4.4	5.8	11.0
Fl Himalayan x Polish	2.0	4.4	7.0	47.4	2.6	4.1	5.6	10.9
Polish	1.4	3.1	3.3	43.4	2.0	3.6	5.2	11.0
Domestic fowl								
(Kempster *et al.*, Missouri) Females								
Rhode Island Red	3.56	7.85	5.2	16.6	2.28	6.5	10.6	25.9
Plymouth Rock	3.40	7.50	5.43	19.5	2.40	6.0	9.5	22.5
Rhode Island White	3.00	6.61	4.65	20.6	2.10	5.5	8.9	21.1
White Leghorn	2.20	4.85	3.25	18.0	2.17	6.0	9.9	23.9
Ancona	1.65	3.64	4.0	34.4	2.57	4.6	6.6	15.0

TABLE 16.1 (*Continued*)

Animal	*A* (Mature Wt.)		*B*	$100k^1$ (Percentage of monthly decline)	t^*	Age² (from conception) at		
						50% mature weight	75% mature weight	98% mature weight
	(*kg.*)	(*lb.*)	(*kg.*)		(*mos.*)	(*mos.*)	(*mos.*)	(*mos.*)
Domestic fowl—Cont.								
(Jull, U. S. D. A.)								
Rhode Island Reds, males	4.6	10.1	6.7	21	1.8	5.1	8.4	20.4
Rhode Island Reds, males	4.2	9.3	5.6	24	1.2	4.1	7.0	17.5
Rhode Island Reds, castrated males	4.2	9.3	5.6	24	1.2	4.1	7.0	17.5
Rhode Island Reds, females	3.6	7.9	5.3	17	2.3	6.4	10.5	23.2
(May R. I. Station)								
Cornish, males	2.8	6.2	4.6	24	2.1	5.0	7.9	18.4
Cornish, females	2.1	4.6	3.2	22	1.9	5.1	8.2	19.7
Hamburg, males	1.7	3.7	2.3	21	1.5	4.8	8.1	20.1
Hamburg, females	1.5	3.3	1.9	17	1.4	5.5	9.6	24.4
(May & Waters, R. I. Station)								
Brahma, males	4.1	9.0	8.1	25.1	2.7	5.5	8.2	18.3
Brahma, females	3.4	7.5	7.0	24.8	2.9	5.7	8.5	18.7
Leghorn, males	2.2	4.9	4.9	33.4	2.4	4.5	6.6	14.1
Leghorn, females	1.8	3.9	4.1	35.0	2.3	4.3	6.3	13.5
L x B males	3.3	7.2	13.7	45.0	3.2	4.7	6.3	11.9
B x L males	3.1	6.9	8.3	35.6	2.8	4.7	6.7	13.8
L x B females	2.3	5.0	13.6	57.5	3.1	4.3	5.5	9.9
B x L females	2.5	5.4	6.4	35.5	2.6	4.6	6.5	13.6
Guinea pig (Castle)								
F_1, Arequipa x Race B, m	1.30	2.87	1.95	19.8	2.05	5.6	9.1	21.8
F_2, Arequipa x Race B, m	1.04	2.29	1.46	20.9	1.62	4.9	8.3	20.5
F_1, Cavia cutleri x Race B males	.930	2.05	1.60	27.4	2.00	4.5	7.0	16.3
Race B, males	.870	1.92	1.45	21.7	2.35	5.55	8.76	20.4
Race B, females	.800	1.76	1.59	24.7	2.6	5.7	8.4	18.5
F_1, C. cutleri x Race B, females	.785	1.73	1.26	26.1	1.8	4.5	7.1	17.0
F_2, C. cutleri x Race B, males	.725	1.60	1.10	25.1	1.66	4.4	7.2	17.5
F_2, cutleri x Race B, females	.590	1.30	1.45	40.5	2.22	3.9	5.6	11.9
C., cutleri, males	.400	.882	1.7	52.9	2.74	4.0	5.4	10.1
C., cutleri, females	.333	.734	.780	43.4	1.96	5.95	6.95	11.0
Norway rat								
(King)								
females	.290	.638	.415	12.9	.89	6.3	11.7	31.2
males	.385	.849	.43	12.2	.906	6.6	12.2	32.4
Albino rat								
Specially well fed & cared for males (Greenman & Duhring)	.350	.772	.65	35.0	1.77	3.75	5.73	12.9
Inbred, 7–15 generation series (King), males	.335	.738	.57	38.3	1.4	3.21	5.00	11.5
females	.215	.474	.42	49.0	1.4	2.6	4.2	9.3

TABLE 16.1 (*Continued*)

Animal	A (Mature Wt.)		B	100*k*[1] (Percentage of monthly decline)	*t**	Age[2] (from conception) at		
						50% mature weight	75% mature weight	98% mature weight
	(*kg.*)	(*lb.*)	(*kg.*)		(*mos.*)	(*mos.*)	(*mos.*)	(*mo*).
On whole milk and whole wheat diet (Sherman & MacLeod).								
males	.330	.728	.80	52.0	1.7	3.03	4.37	9.3
females	.223	.492	.88	70.7	1.94	2.92	3.90	7.5
inbred, 16–25 generation series (King).								
Males	.320	.705	.470	29.1	1.33	3.70	6.08	14.7
Females	.217	.478	.350	38.3	1.25	3.05	4.87	11.3
Stock rats (Donaldson *et al.*)								
Males (Stock rats)	.280	.617	.59	40.0	1.86	3.59	5.33	11.6
Females (Ferry)	.203	.447	.75	64.4	2.03	3.11	4.18	8.1
Control rats for inbreed-	.270	.595	.450	34.1	1.50	3.55	5.56	13.0
ing experiments (King)	.172	.379	.280	41.8	1.17	2.8	4.5	10.5
Males	.255	.562	.400	33.0	1.36	3.46	5.57	13.1
Females	.189	.417	.280	35.7	1.10	3.0	5.0	10.9
Stock rats (King)								
Females	.210	.463	.39	48.5	1.28	2.7	4.1	9.3
Stock rats (Hoskins)								
Males	.230	.507	.86	81.0	1.63	2.5	3.3	6.5
Females	.166	.366	.60	88.5	1.5	2.2	3.0	5.8
"Runt" (Series 1, No. 1) (King)								
Female	.147	.324	.33	62.1	1.3	2.4	3.5	7.5
Normal litter mate to runt (Series 1, No. 3)								
Female	.170	.375	.460	70.7	1.4	2.4	3.4	6.9
White mouse								
(Robertson)								
Males	.0275	.061	.044	62.0	.76	1.88	3.01	7.10
Females	.0235	.052	.050	82.0	.92	1.76	2.60	5.7
Albino Mouse								
(Robertson & Ray, 1925)								
Males	.026	.057	.053	67.2	1.03	2.1	3.1	6.9
Females	.0228	.050	.041	63.9	.88	2.0	3.1	7.0
Pigeon								
(Riddle & Frey)								
Common pigeon, male & female	.340	.750	1.40	80	.139	2.6	3.5	6.7
Ring dove, male & female	.160	.353	.006	102[3]	.06	.74	1.4	3.9

TABLE 16.1 (*Concluded*)

Man	*A* (Mature Wt.)		*B*	100k[1] (Percentage of monthly decline)	t^*	Age[2] (from conception) at 50% mature weight	75% mature weight	98% mature weight
	(*kg.*)	(*lb.*)	(*kg.*)		(*mos.*)	(*yrs.*)	(*yrs.*)	(*yrs.*)
Man								
Males								
English non-laboring classes (Stephenson)	69.2	152.6	183808	4.8	13.68	12.3	16.1	20.5
English all classes (Roberts)	68.0	149.9	5043	2.98	12.03	12.4	15.9	23.0
Swedish (Key)	68.0	149.9	22851	3.62	13.4	12.4	16.6	22.4
U. S. naval cadets (Beyer)	65.8	145.1	2156	3.68	13.1	....	16.2	22.0
U. S. Amherst College & Neb. students (Hastings)	65.4	144.2	7113	3.14	12.44	12.7	16.1	22.8
English laboring classes (Stephenson)	65.3	144.0	2037	2.38	12.1	12.3	17.0	25.8
Polish Radom Gymnasium (Suligowski)	62.0	136.7	15782	3.76	12.28	11.4	15.4	21.0
English artisan classes (Roberts)	61.6	135.8	13309	3.46	12.9	11.3	16.3	22.4
Russian St. Petersburg School (Wiazemsky)	61.5	135.6	79447	4.45	13.4	12.3	16.0	20.7
Jews in South Russia (Weissenberg)	58.0	127.9	171302	4.76	14.0	12.3	16.5	20.9
Chinese students in Wuchang School (Merrins)	55.0	121.3	6301	3.31	11.9	12.6	15.4	21.8
Philippine (Bobbitt)	52.3	115.3	15326	3.83	12.4	12.0	15.4	20.9
Japanese (Miwa)	51.4	113.3	39694	4.46	12.4	11.7	15.0	19.7
Females								
English (all classes) (Roberts)	57.4	126.6	1331	2.6	10.1	11.1	14.5	22.6
American well to do, New York (Baldwin)	56.4	124.4	7944	3.97	10.4	10.1	13.3	18.6
Russian Institutions (Diek)	54.0	119.1	1398	2.66	10.2	....	14.5	22.5
German (Camerer)	51.6	113.8	12430	4.08	11.2	10.4	14.1	19.2
Japanese (Miwa)	46.0	101.4	2751	3.36	10.2	....	13.6	19.9

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[1] The percentage of monthly persistency of growth, 100P, may be obtained by subtracting the percentage decline, 100k, from 100; i.e., 100 P = 100 − 100 k.

[2] By age is meant, in all cases, are as counted from conception. The following ages of the animals at birth are given should the reader desire to convert the conceptional ages to birth ages: Cattle 9.4 mos., horse 11 mos., swine 4.0 mos., sheep 5.0 mos.; rabbit 1.0 mos.; fowl 0.7 mos. (21 days); guinea pig 2.2 mos. (67 days); mouse 0.66 mos. (20 days); pigeon 0.6 mos. (18 days); man 0.79 yrs. (9.5 mos.).

TABLE 16.2 GROWTH OF DAIRY CATTLE

	HOLSTEIN FEMALES									JERSEY FEMALES							
Age Mos.	Weight		Height at withers		Circumference of chest		Width of hips		Age Mos.	Weight		Height at withers		Circumference of chest		Width at hips	
	No. of animals	lbs.	No. of animals	inches	No. of animals	inches	No. of animals	inches		No. of animals	lbs.	No. of animals	inches	No. of animals	inches	No. of animals	inches
Birth	239	90	169	29.1	81	30.8	81	6.7	Birth	173	53	100	25.7	58	27.4	58	5.7
1	237	112	207	30.6	87	33.9	123	7.3	1	151	67	137	27.0	62	29.8	98	6.0
2	237	148	218	32.3	87	37.0	132	8.4	2	159	90	145	28.9	62	32.5	104	6.8
3	234	193	215	34.3	85	39.9	130	9.2	3	158	121	145	30.6	61	35.4	104	7.7
4	234	243	212	36.2	85	42.9	130	10.1	4	159	158	146	32.6	61	38.1	105	8.5
5	233	297	214	37.7	86	46.0	133	11.1	5	166	199	153	34.5	63	40.9	110	9.4
6	231	355	213	39.7	84	48.7	131	11.9	6	167	243	154	36.2	63	43.7	111	10.3
7	229	410	210	41.1	82	51.1	129	12.7	7	167	286	154	37.7	62	46.3	111	11.0
8	224	462	205	42.3	77	53.2	124	13.4	8	167	324	154	39.0	62	48.4	111	11.7
9	217	509	199	43.5	73	54.6	119	14.0	9	163	360	150	40.1	61	50.1	110	12.4
10	213	552	195	44.4	71	56.3	117	14.5	10	163	393	150	40.9	60	51.5	110	13.4
11	204	593	186	45.3	63	58.2	109	15.1	11	160	420	147	41.7	59	52.8	108	13.3
12	200	632	183	46.0	59	58.9	106	15.5	12	159	450	146	42.2	56	54.0	106	13.7
13	197	671	181	46.7	57	59.8	104	15.8	13	141	479	145	42.8	55	55.3	106	14.1
14	191	705	178	47.3	56	61.4	103	16.2	14	147	507	136	43.3	48	56.3	99	14.5
15	185	746	173	47.9	51	62.6	98	16.5	15	143	530	132	43.9	46	57.5	98	14.9
16	185	782	173	48.5	50	63.6	97	16.9	16	138	558	127	44.4	43	58.6	95	15.2
17	174	809	162	48.9	47	64.2	93	17.2	17	134	580	125	44.7	42	59.5	94	15.6
18	165	845	153	49.3	43	64.9	89	17.5	18	129	601	121	45.2	40	60.0	92	15.8
19	159	878	147	49.8	42	65.5	88	17.8	19	127	622	121	45.5	40	61.1	92	16.0
20	154	912	142	50.2	41	66.7	86	18.1	20	125	642	120	45.9	40	61.9	92	16.4
21	150	952	138	50.6	39	67.9	84	18.3	21	123	665	118	46.2	38	62.8	89	16.5
22	154	986	141	51.0	41	68.8	85	18.7	22	120	684	115	46.4	36	63.8	87	16.8
23	147	1024	134	51.3	37	70.1	78	19.2	23	117	708	112	46.7	37	64.5	88	17.1
24	140	1069	131	51.7	35	71.3	80	19.4	24	118	733	113	46.9	36	65.3	87	17.5
27	81	1151	69	52.2	35	74.0	69	20.3	27	77	816	64	47.7	36	67.0	64	18.1
30	79	1120	61	52.5	33	72.5	61	20.4	30	82	824	65	47.9	39	67.5	65	18.5
33	81	1130	61	52.7	34	72.5	61	20.7	33	80	832	65	48.0	39	67.8	65	18.7
36	75	1165	55	53.0	28	73.8	55	21.0	36	77	855	60	48.2	37	68.2	60	19.0
39	69	1176	50	53.1	26	74.3	50	21.1	39	70	899	53	48.6	34	69.2	53	19.5
42	64	1202	46	53.2	22	75.3	46	21.4	42	61	895	48	48.6	28	69.1	48	19.5
45	58	1197	40	53.2	20	74.7	40	21.6	45	55	898	40	48.5	21	68.9	40	19.7

TABLE 16.2 (*Continued*)

48	48	1232	31	53.3	12	75.2	31	21.8	48	49	897	35	48.5	18	68.7	35	19.8
51	46	1261	31	53.5	12	76.6	31	22.1	51	42	927	30	48.5	15	70.1	30	19.9
54	43	1271	28	53.6	10	76.9	28	22.1	54	39	952	28	48.6	13	70.5	28	20.0
57	41	1305	30	53.7	9	77.0	30	22.6	57	40	944	30	48.6	12	70.2	30	19.9
60	41	1330	27	53.6	8	76.3	27	22.5	60	36	937	26	49.0	9	69.8	26	20.1
63	51	1310	36	53.5	17	76.2	36	22.5	63	57	948	45	49.0	29	70.2	45	20.3
66	44	1312	30	53.7	16	76.7	30	22.6	66	46	955	36	48.7	20	70.9	36	20.2
69	45	1343	31	53.7	18	77.6	31	22.8	69	43	966	32	48.6	16	71.0	32	20.4
72	45	1317	31	53.7	18	76.3	31	22.8	72	38	973	29	48.4	14	70.8	29	20.2
75	37	1320	24	53.9	12	77.2	24	22.7	75	36	964	29	48.5	16	70.1	29	20.1
78	33	1357	20	54.0	8	78.3	20	23.0	78	36	998	27	48.6	15	71.1	27	20.3
81	30	1400	17	53.8	6	79.6	17	22.9	81	31	991	21	48.4	12	70.6	22	20.3
84	27	1401	17	53.7	6	76.5	17	23.0	84	25	959	18	48.0	9	70.7	18	20.3
87	25	1402	16	53.6	6	78.6	16	23.1	87	21	952	14	48.3	7	69.9	14	19.9
90	29	1358	16	53.7	6	79.0	16	23.0	90	21	1002	13	48.2	6	72.8	13	20.1
93	25	1335	13	53.5	6	80.3	13	22.8	93	18	984	12	48.4	5	73.0	12	20.0
96	24	1365	12	53.2	6	80.4	12	22.9	96	13	909	5	47.7	. .	. . . .	5	19.6

GUERNSEY FEMALES

Age Mos.	Weight		Height at withers		Width at hips	
	No. of animals	lbs.	No. of animals	inches	No. of animals	inches
Birth	108	65	38	26.6	. .	. . . .
1	82	77	75	28.2	37	6.1
2	86	102	79	29.8	40	6.9
3	86	133	78	31.6	40	7.7
4	86	173	78	33.5	40	8.7
5	87	216	79	35.3	41	9.4
6	86	260	78	36.9	41	10.1
7	86	305	75	38.4	38	11.0
8	85	350	76	39.9	39	11.7
9	88	389	79	40.9	40	12.3
10	85	427	76	41.7	40	12.9
11	87	459	79	42.6	40	13.3
12	87	490	79	43.3	40	13.7
13	88	524	80	43.9	41	14.2
14	88	556	80	44.6	41	14.6

AYRSHIRE FEMALES

Age Mos.	Weight		Height at withers		Circumference of chest		Width at hips	
	No. of animals	lbs.	No. of animals	inches	No. of animals	inches	No. of animals	inches
Birth	124	72	97	27.6	15	28.9	15	6.1
1	122	89	123	28.6	15	31.1	42	6.5
2	123	119	123	30.2	15	34.3	43	7.2
3	123	158	123	31.9	15	37.6	43	8.3
4	120	198	120	34.0	15	40.8	43	9.3
5	118	245	118	35.5	15	43.2	43	10.1
6	119	293	119	37.2	15	45.4	42	10.9
7	117	344	117	38.5	15	47.9	42	11.7
8	113	389	113	39.9	14	50.2	40	12.5
9	112	433	112	40.9	14	51.3	40	13.0
10	112	469	112	41.7	14	52.8	40	12.6
11	113	502	113	42.5	14	54.2	41	13.8
12	114	538	114	43.2	14	55.7	41	14.3
13	113	577	113	44.0	13	56.6	40	14.7
14	113	611	113	44.8	13	57.8	40	15.1

TABLE 16.2 (*Continued*)

	Guernsey Females							Ayrshire Females							
Age Mos.	Weight		Height at withers		Width at hips		Age Mos.	Weight		Height at withers		Circumference of chest		Width at hips	
	No of animals	lbs.	No of animals	inches	No. of animals	inches		No. of animals	lbs.	No. of animals	inches	No. of animals	inches	No. of animals	inches
15	85	584	77	45.0	40	14.9	15	108	638	108	45.1	13	59.3	38	15.5
16	85	605	77	45.3	43	15.2	16	101	669	101	45.7	10	59.6	36	15.8
17	87	634	79	45.9	43	15.4	17	95	697	95	46.2	10	60.5	36	16.1
18	82	663	74	46.4	41	15.8	18	94	725	94	46.5	9	61.3	35	16.3
19	80	686	73	46.7	42	15.9	19	94	758	94	46.8	9	61.4	36	16.7
20	79	712	72	47.0	42	16.1	20	96	793	95	47.4	9	63.3	37	16.8
21	78	737	71	47.3	42	16.5	21	92	818	91	47.6	9	63.3	37	17.2
22	74	763	68	47.7	41	16.7	22	81	844	90	47.8	9	64.6	36	17.4
23	71	788	67	47.9	40	17.1	23	86	871	86	48.1	9	64.8	36	17.6
24	67	818	63	48.0	38	17.3	24	87	902	86	48.3	9	66.3	35	18.0
27	29	876	23	48.9	23	18.2	27	35	909	31	48.1	8	68.1	35	18.7
30	29	880	20	49.3	20	18.5	30	34	945	30	48.3	8	67.9	34	19.1
33	29	905	18	49.7	18	18.7	33	31	965	25	48.9	6	70.3	31	19.6
36	29	901	16	49.9	16	19.1	36	28	968	23	48.7	5	70.0	28	19.8
39	29	924	16	50.0	16	19.3	39	25	1007	19	49.1	5	71.2	25	20.0
42	28	952	16	49.9	16	19.6	42	25	1014	20	49.9	6	71.0	25	20.4
45	29	971	15	50.1	15	19.8	45	20	1038	16	50.0	3	71.3	20	20.6
48	25	990	12	50.4	12	19.7	48	19	1035	15	50.2	3	72.0	19	20.6
51	23	980	11	50.6	11	19.9	51	20	1040	15	49.4	3	70.9	20	20.7
54	21	1024	11	50.5	11	20.2	54	18	1058	13	50.3	3	71.7	18	20.5
57	25	1031	13	50.5	13	20.2	57	21	1073	15	50.3	3	76.1	21	20.8
60	25	1055	11	50.6	11	20.0	60	20	1080	15	50.4	3	74.9	20	21.0
63	24	1043	10	50.4	10	19.9	63	21	1037	16	49.2	6	71.9	16	22.8
66	20	1051	8	50.0	8	20.0	66	19	1055	14	49.2	6	72.7	14	20.2
69	19	1073	7	49.8	7	20.1	69	18	1088	13	49.3	6	75.5	13	21.0
72	15	1093	6	49.7	6	20.3	72	16	1132	12	49.1	5	73.9	12	20.9
75	16	1042	5	49.3	5	19.5	75	14	1067	9	48.3	3	69.3	9	20.3
78	14	1084	5	49.4	5	19.8	78	13	1080	9	48.9	2	69.9	9	20.5
81	15	1071	5	49.2	5	19.6	81	13	1092	9	49.1	2	72.4	9	20.8
84	16	1066	5	49.3	5	19.5	84	9	1122	9	48.7	..	....	5	20.7
87	16	1065	5	49.4	5	19.7	87	9	1109	5	48.8	..	....	5	21.0
90	14	1053	4	49.4	4	19.7	90	8	1103	4	48.7	..	....	4	20.4
93	13	1067	4	48.9	4	19.6	93	8	1083	4	48.5	..	....	4	20.4
96	13	1070	4	49.6	4	19.7	96	7	1143	3	49.2	..	....	3	21.0

TABLE 16.2 (*Concluded*)

HOLSTEIN MALES							JERSEY MALES						
Age Mos.	Weight		Height at withers		Circumference of chest		Age Mos.	Weight		Height at withers		Circumference of chest	
	No. of animals	lbs.	No. of animals	inches	No. of animals	inches		No. of animals	lbs.	No. of animals	inches	No. of animals	inches
Birth	159	94	159	29.4	89	31.3	Birth	100	60	100	26.2	65	27.9
1	159	125	159	31.2	90	34.1	1	99	78	99	27.9	66	30.1
2	159	164	159	33.2	90	37.3	2	97	104	97	29.7	66	32.8
3	152	214	152	34.8	88	40.6	3	97	141	97	31.5	66	35.9
4	146	269	146	36.4	87	43.9	4	97	184	97	33.6	66	39.4
5	131	336	131	38.8	77	47.2	5	92	233	92	35.5	65	42.6
6	120	399	120	40.5	69	50.0	6	82	282	82	37.2	58	45.2
7	104	456	104	41.9	61	52.6	7	65	326	65	38.4	42	47.4
8	88	514	88	43.1	54	54.7	8	55	371	55	39.5	34	49.7
9	70	563	70	44.2	42	56.6	9	46	410	46	40.4	28	52.0
10	53	620	53	45.1	35	58.7	10	39	452	39	41.4	22	53.9
11	46	683	46	46.4	31	60.6	11	30	497	30	42.7	20	55.4
12	35	741	35	47.5	25	62.5	12	23	531	23	43.0	15	56.9
13	16	796	16	48.2	16	64.4	13	13	566	13	43.9	13	58.3
14	13	870	13	48.8	13	66.1	14	11	613	11	45.0	11	59.5
15	7	978	7	49.7	7	69.1	15	9	643	9	45.5	9	60.7
16	3	1035	3	50.5	3	71.7	16	8	679	8	46.1	8	62.2
17	3	1090	3	50.7	3	72.7	17	7	726	7	47.0	7	63.6
18	2	1176	2	52.2	2	74.4	18	5	745	5	47.5	5	64.3
19	2	1236	2	53.3	2	75.2	19	4	826	4	48.4	4	67.7
20	2	1286	2	53.3	2	76.0	20	4	856	4	48.6	4	67.5
21	2	1345	2	54.3	2	76.6	21	3	875	3	48.9	3	68.1
22	2	1364	2	54.3	2	77.4	22	3	904	3	49.3	3	68.2
23	2	1410	2	54.9	2	78.5	23	3	931	3	50.0	3	71.2
24	2	1438	2	55.9	2	78.9	24	3	969	3	50.3	3	71.0

Chapter 17

Linear Growth, Form, and Function

> Geometric laws determine physiologic processes. *G. Teissier*
>
> The more the organism changes the more it remains the same. *A. H. Hersh*
>
> Remember that "formative substances", hormones, vitamins, genes, and similar controlling agencies, are merely mechanisms of a more deeply seated control which knits the mass of living stuff into an organism. We seek the architect, not the maker of builder's supplies. *E. W. Sinnott*

17.1: Introduction and definitions. The basic problem of organization is how genetically identical cells give rise to histologically diverse ones, and how growth occurs at different rates in different directions resulting in differences in size, form, and function. Many factors have been investigated and found to be influential: genes, hormones, auxins, organizers, evocators, competency, morphogenetic fields, organic gradients, electrical fields, electric currents, light, gravity, heat, mechanical pressure, enzymes, sulfhydryl, minerals, vitamins, proteins, amino and nucleic acids, fats, carbohydrates, and so on. There is an enormous literature[1] on these influential factors and mechanisms, some of which are discussed elsewhere in this book. The present chapter is not concerned with these factors, but, like the preceding chapter, with the numerical relationships of part to whole during increase in size, and with very general explanations concerning the interrelationships between size, form, and function[2]. These problems have very important relations to agriculture and nutrition, as illustrated by the preoccupation of animal husbandmen with livestock judging (see below).

Let us then discuss the general problem of change in form with increasing age.

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[1] See, among many others, Needham's books and reviews; the Symposia on "Development and Growth," published in the supplements to the journal *Growth*. Waddington, C. H., "Organizers and genes," Cambridge Univ., 1940. Sinnott, E. W., and Dunn, L. C., "Genes and development of size and form," *Biol. Rev.* **10,** 123 (1935). Sinnott, *Am. Naturalist*, **76,** 253 (1942). Goldschmidt, R., "Physiological genetics," McGraw-Hill Book Co., 1938, and "The material basis of evolution," Yale Univ. Press, 1940. Weiss, P., "Principles of development," N. Y., 1939. Burr, H. S., "Electrodynamic theory of development," *J. Comp. Neurol.*, **56,** 347 (1932). Gurwitch, A., *Embryonalen Feld. Arch. Entw. Mech.*, **51,** 383 (1922). Harrison, R. G., "Determination Problems," *Am. Naturalist*, **67,** 306 (1933). Child, C. M., "Patterns and problems of development," Univ. Chicago Press, 1941. Wendt, F. W., and Thimann, K. V., "Phytohormones," N. Y., 1937.

[2] Thompson, D'Arcy W., "On growth and form," Cambridge Univ. Press, 1917 (new ed. 1942).

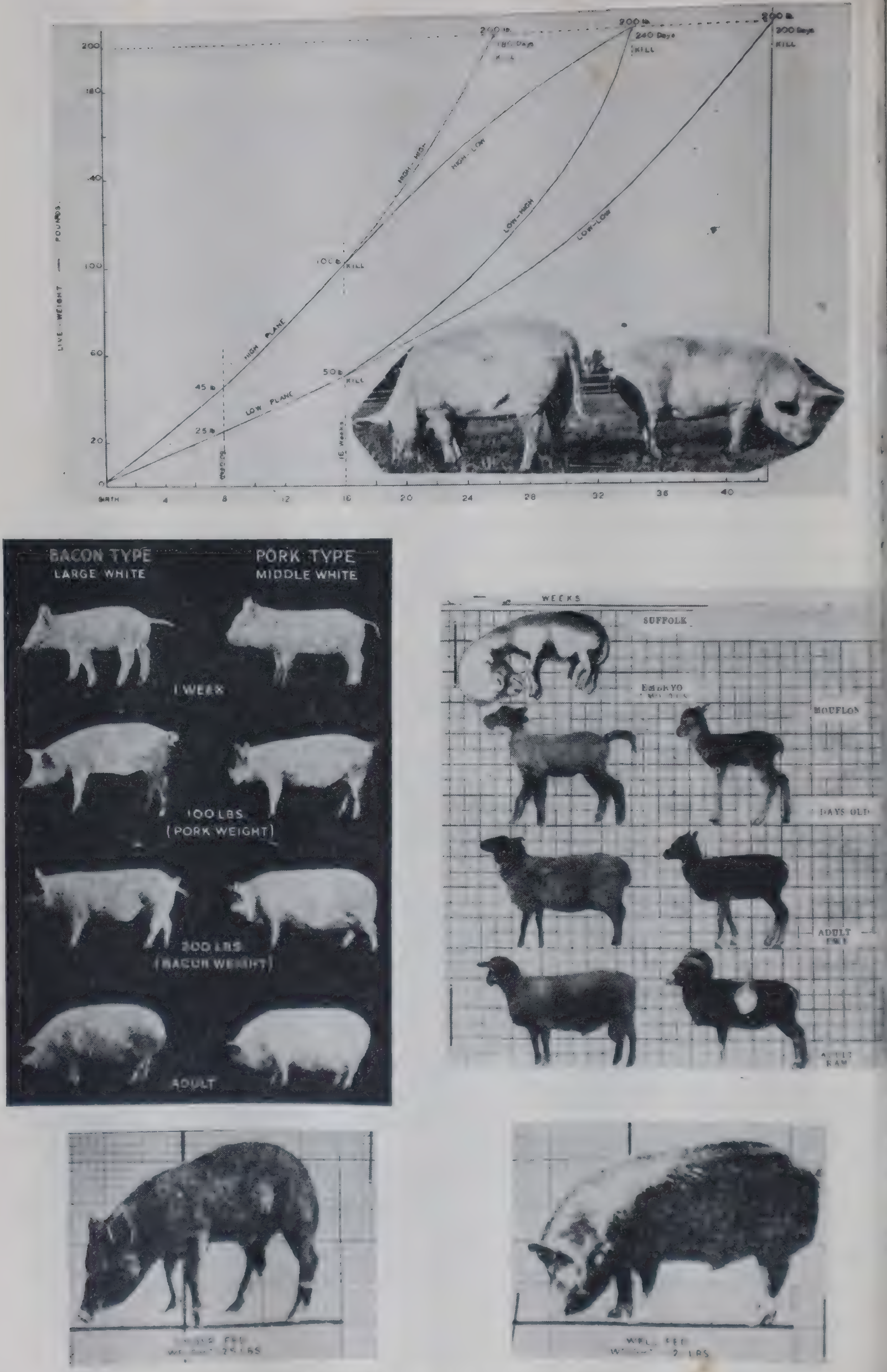

Fig. 17.1a (caption next page)

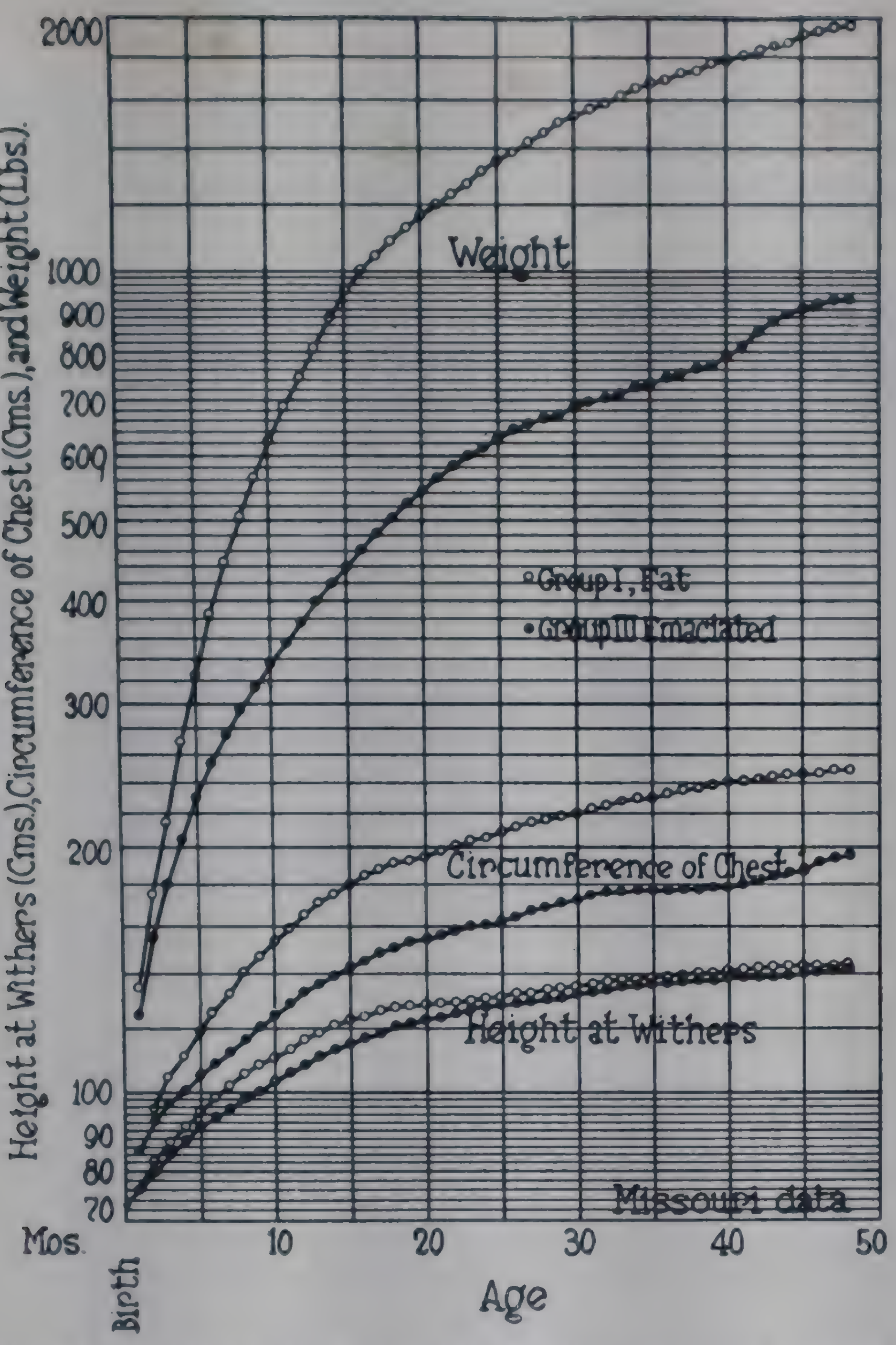

Fig. 17.1b. Weight, chest girth, and height at withers of full-fed and under-fed steers plotted against age on arithlog paper. Note the *relative* rate of increase of these three indices of size, and the influence of the plane of nutrition on them.

Fig. 17.1a. Influence of nutrition and selection on change in bodily proportions. The charts are from reprints sent to the writer by John Hammond, Cambridge University. Photographs of all animals were reduced to the same height at shoulder so as to compare change in proportions as distinct from change in size. Note that the body proportions of the pork type at 100 lb are the same as of the bacon type at 200 lb. Note the difference in proportions in under-fed and well-fed. Note the various methods of approaching to body weight 200 lb, and photograph of animals raised up to 200 lb by two different methods ("high low" and "low-high") with differences in "type" thereafter. Differences in food supply at different ages accelerates selectively, the early or late developing tissues thus changing bodily proportions. References to Hammond, McMeekan and associates are given in the text.[9] For the pig charts, see especially C. P. McMeekan and J. Hammond, *Empire J. Exp. Agr.*, **8,** 8 (1940), and *J. Ministry of Agric.*, **46,** 238 (1939); and Hammond, J., *J. Roy. Agr. Soc. England*, **93,** 1 (1933). For the sheep, Hammond, *The Farmer and Stock Breeder Agricultural Gazette* (England), Dec. 10, 1928. Note that in the improved breed of sheep (left) the changes in bodily proportions are pushed to a further "stage" than in the wild type (right). This is true of other domestic animals selected for "further stages" of development at earlier ages. What was accomplished by selection and selective feeding, may perhaps be accomplished by other methods (hormone administration, etc.).

In geometrically similar bodies[3], such as small and large spheres, surface, S, is proportional to the square of linear size, L, and volume or weight, V or W, is proportional to the cube of linear size, as shown by equations (17.1)[4]:

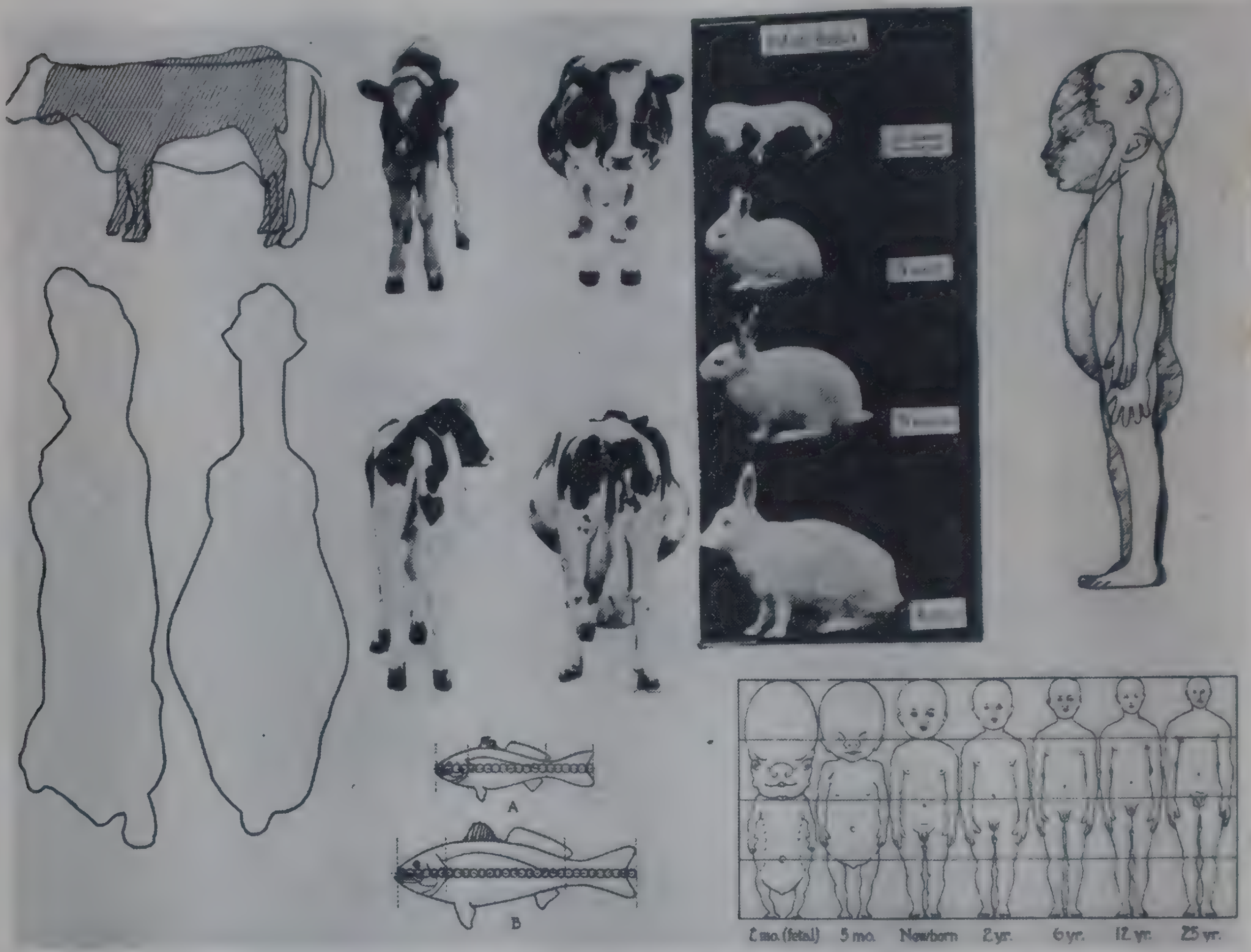

Fig. 17.1c. Marine animals (small and large fish) were apparently not under the compulsion of gravity (and other factors) to change in external body form; land animals apparently were under such compulsions as indicated, for example, by the relatively larger heads in the new-born land species. New-born cattle, sheep, goats, horses, and related species have long legs and short, shallow bodies. On maturing, especially in the improved meat breeds, the buttocks and loins grow at a faster rate than the head and legs. The greater the "improvement" the more rapid the relative increase in these "meat parts." Sources of data: Dairy cattle, original (photographs reduced to the same height at withers). Rabbit, from John Hammond, Yearbook National Rabbit Council, England, 1931 (photographs reduced to the same cranium size to show increase in body in contrast to that of the head). Fish, from Hecht, and man, from Strantz, both as cited by C. M. Jackson in the book "Growth," by W. J. Robbins, S. Brody, C. M. Jackson, A. G. Hogan and C. W. Green, Yale Press (1928). For man, see also Edith Boyd: "Outline of Physical Growth and Development," Burgess, Minneapolis, Minn. (1941).

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[3] A large body is *geometrically similar* to a small body if all the linear dimensions of the large body have the same proportions to one another as those of the small body. Thus, for a large cylinder which has double the diameter of a small one to be geometrically similar to the small, it is necessary that the length of the large cylinder also be double that of the small cylinder.

[4] The growth of a spherical organism:

Diameter	1	2	3	4
Surface Area	1	4	9	16
Volume (weight)	1	8	27	64

Spherical organisms cannot attain a large size because the surface cannot keep up with the volume.

$$S \propto L^2 \text{ and } W \propto L^3 \tag{17.1}$$

Since from the above relation

$$L \propto W^{\frac{1}{3}} \text{ and } S \propto L^2,$$

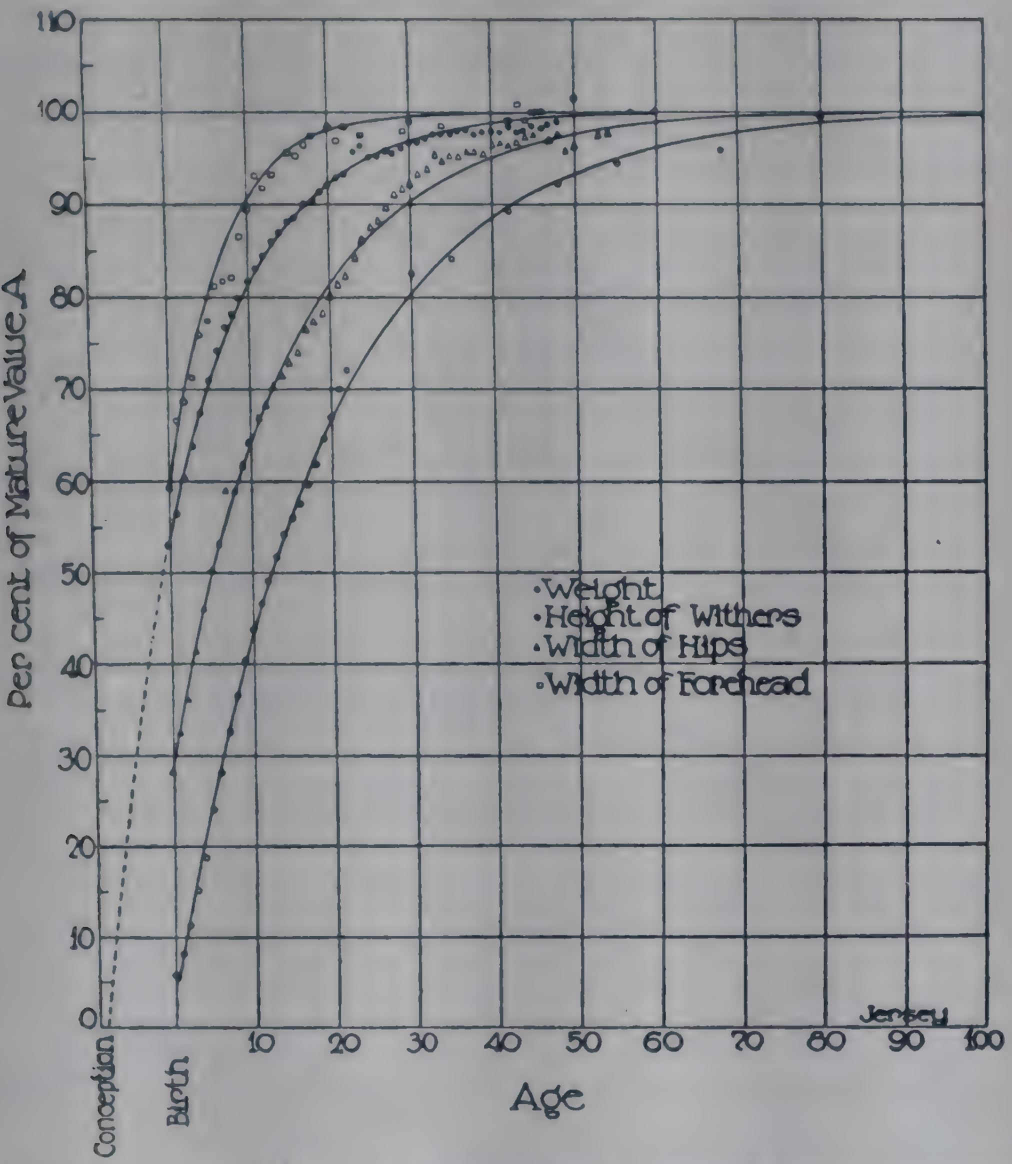

Fig. 17.1d. Age curves of growth in weight and in several skeletal structures plotted in terms of percentage of maximum size. All these age curves follow the same equation, $Y = A - Be^{-kt}$ (in which Y is size at age t and A is maximum size), but the rate, k, of approach to maturity, A, is different for each of these structures. These differences in the rate of approach to maturity lead to change in form with increasing age. While each structure approaches maturity at a rate characteristic of the given structure, different from the rates of growth of other structures, yet the ratio between the percentage change in weight and linear size is approximately constant, b, as indicated by the equation $Y = aX^b$, in which Y is weight, or size of any structure and X is the size of any other structure. Dairy Cattle.

therefore,

$$S \propto (W^{\frac{1}{3}})^2 = aW^{\frac{2}{3}} \tag{17.2}$$

Equation 17.1 shows that during the growth of a body its surface size tends to increase more rapidly than its linear size, and that its volume, or weight size, tends to increase more rapidly than its surface size. Equation (17.2) shows that the surfaces of the body tend to increase, by *geometric necessity*, with the ⅔ power of weight, $W^{\frac{2}{3}}$. However, necessity for physiologic homeostasis (Ch. 10) tends to modify the geometric relations in growing

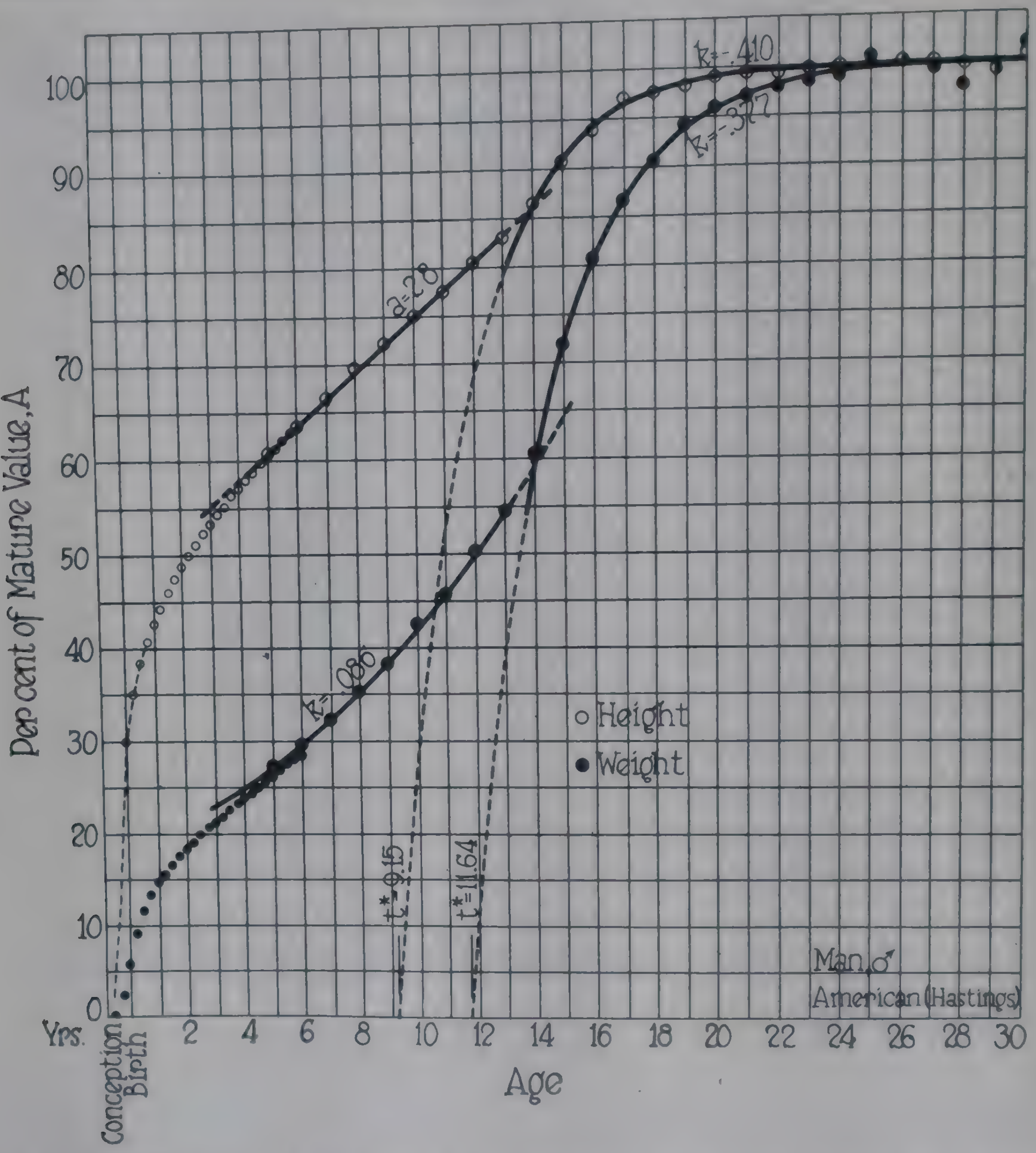

Fig. 17.1e. Differences in the rate, k, of approach to mature height and weight in American boys. Both weight and height at given ages are expressed as percentages of the mature values. Note that this chart may be used for predicting future weights or heights. At 9 years, for example, a boy attains 38 per cent and at 12 years 50 per cent of the mature weight. Therefore, if a boy weighs 23 kg at 9 years, his mature weight will be $23 \times \frac{100}{38} = 60.5$ kg; at 12 years he will weigh $23 \times \frac{50}{38} = 30.3$ kg or $60.5/2 = 30.3$ kg, and so on.

animals. Large and small animals are not similar geometrically but rather tend to be physiologically, *i.e.*, homeostatically, similar. The organism changes geometrically so as to remain the same physiologically. The age curves of growth in different dimensions or in different components tend to be so adjusted as to give the animal mechanical stability and metabolic or physico-chemical homeostasis. The general discussion may be illustrated by a few concrete examples.

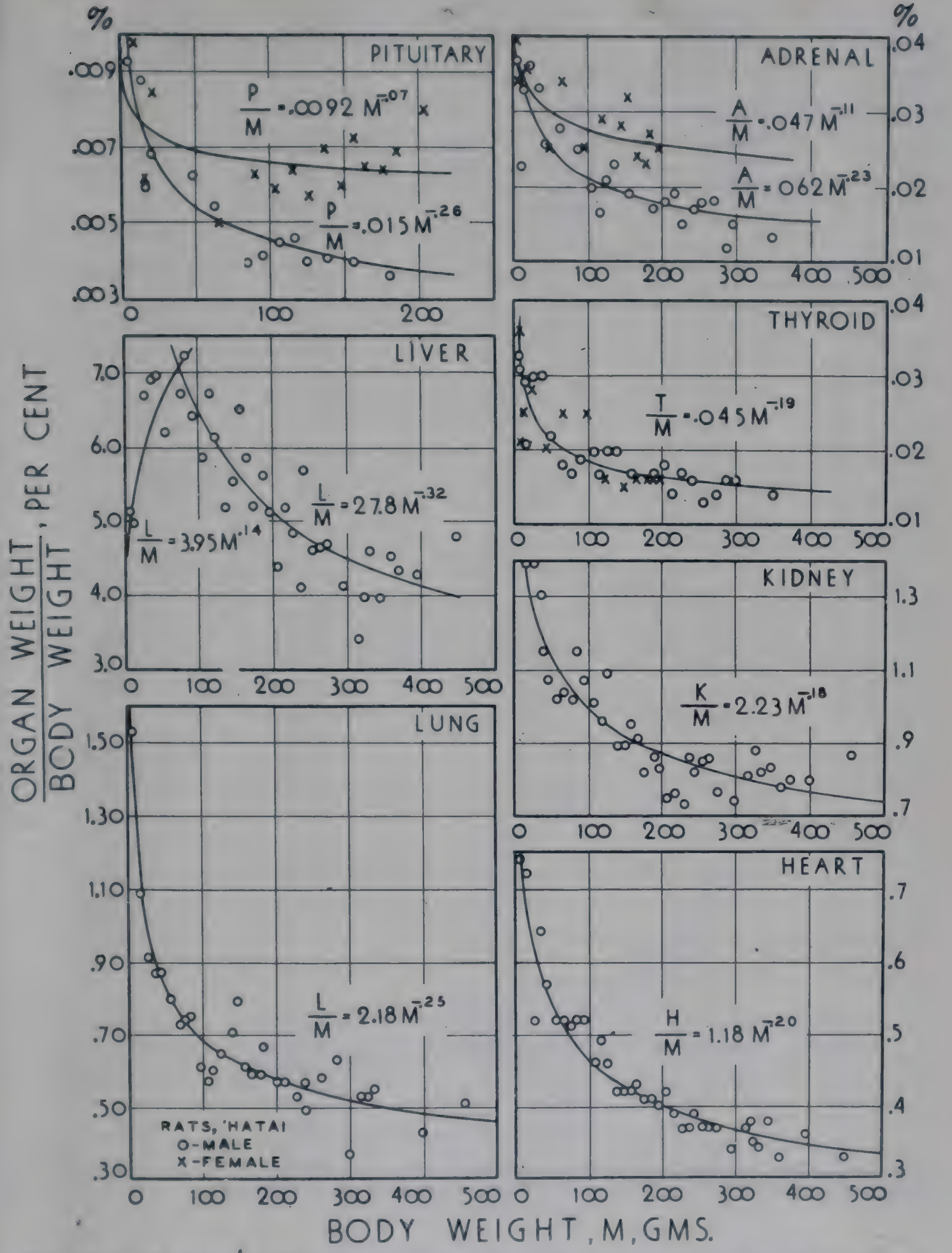

Fig. 17.2a. Relative growth in terms of percentage of one organ, Y, to another or to body weight, X, plotted against age on arithmetic paper. Note the break in the liver curve.

The surfaces are involved in all metabolic processes, including digestion, assimilation, respiration, excretion, secretion, including secretion of hormones. Heat dissipation, likewise, occurs by way of the surface portals (Chs. 11, 13). The metabolic processes, therefore, tend to become ever more cramped with increasing size of the body; they tend to decline per unit weight of body; indeed, they tend to be proportional to the square of the linear size, that is to surface area, $W^{\frac{2}{3}}$. This is not a uniquely biologic phenomenon. The power of an engine likewise tends to vary with the square of its linear size, with its surface area, $W^{\frac{2}{3}}$, rather than with its weight, $W^{1.0}$. This is a basic geometric interrelation as indicated in footnotes 3 and 4.

Then, too, while the weight of a body increases with the cube of its linear size, the strength of its supporting structures, such as of the legs, tends to increase with the cross-section areas of these structures, that is, with $W^{\frac{2}{3}}$. Here mechanical strength and stability tend to decline with increasing size.

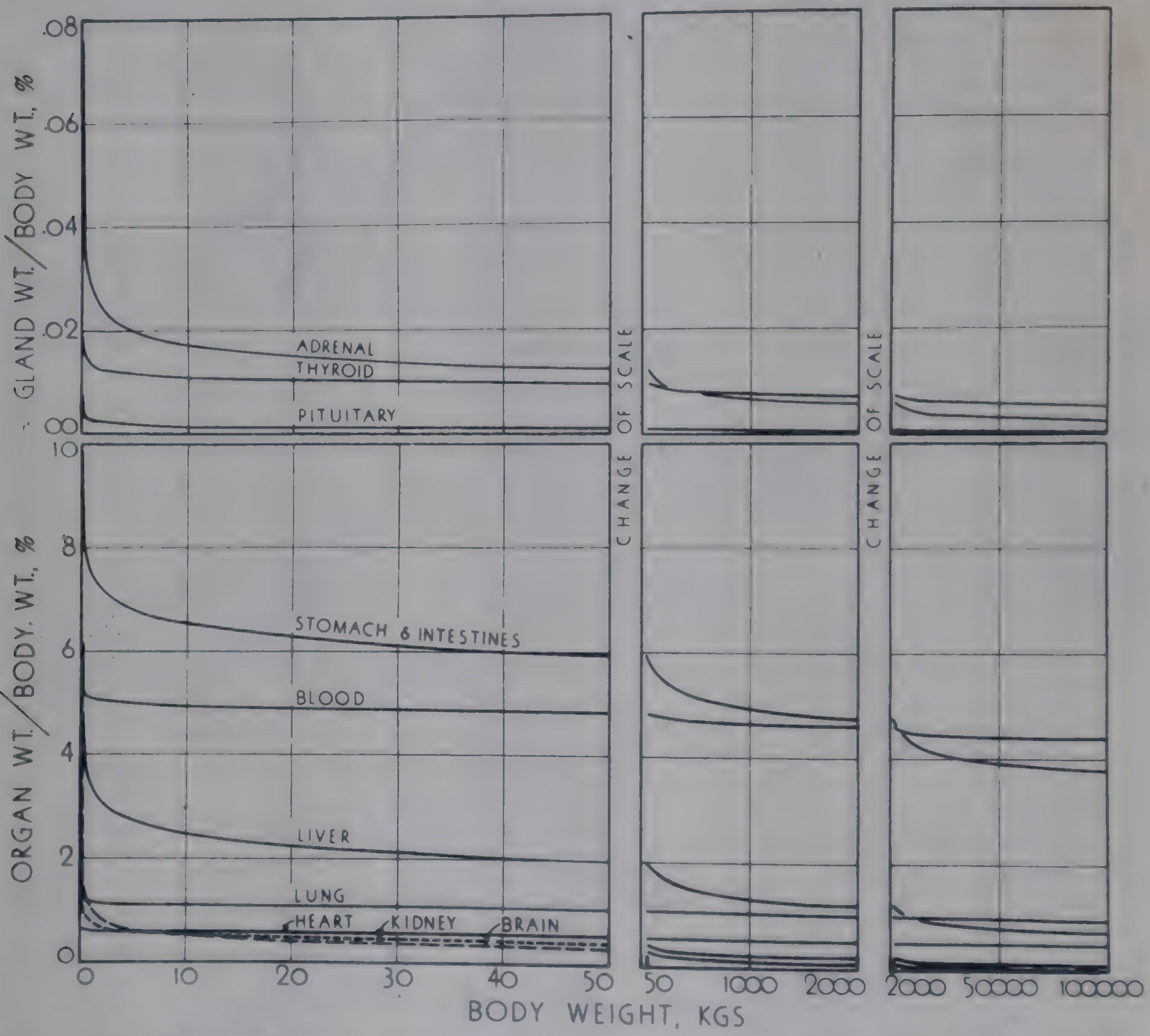

Fig. 17.2b. Ratio of organ weight to body weight plotted against body weight on arithmetic paper. The scales have to be frequently changed in order to crowd in all data. Arithmetically divided paper does not permit plotting significantly wide ranges of data.

In the course of time several devices were evolved to compensate for the decline in the ratios of surface to weight and strength to weight. The decline in the surface-to-weight ratio is compensated, in part, as illustrated by the kidney and lung structures, by various types of folding, packing, invagination, convolution, coiling, and so on. The decline in the ratio of strength to weight is compensated in part by relatively larger increases in the size of the supporting structures than in the non-supporting visceral organs. Thus it comes about that per unit total body weight larger animals have larger muscles and bones than internal organs; or what is the same, the larger the animal the smaller the ratio of visceral-organ weight to body weight.

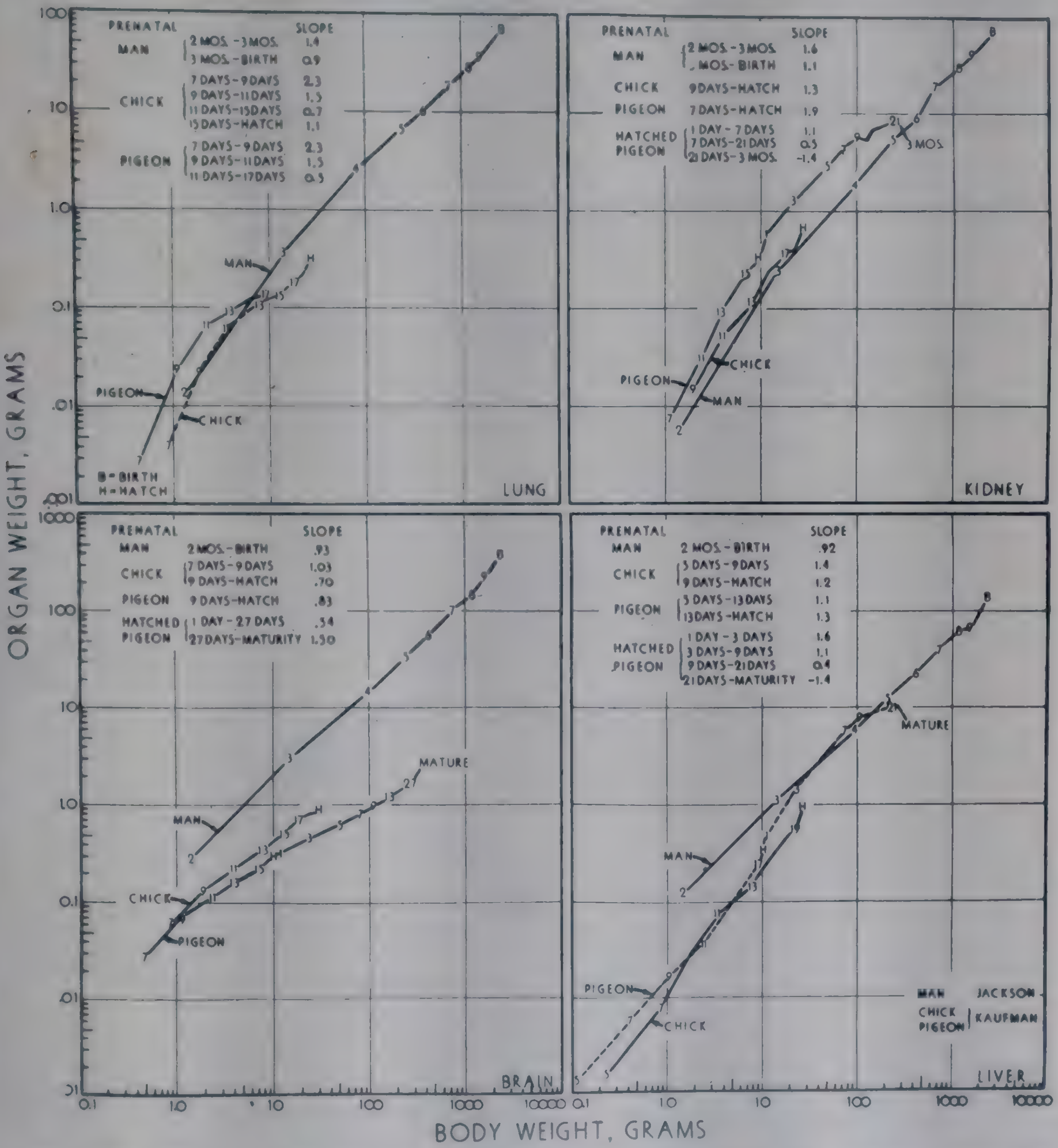

Fig. 17.3. Organ weight (lung, kidney, brain, liver) plotted against body weight for prenatal growth. The numerical values of the exponents or slopes in the equation $Y = aX^b$ are given for several intervals. Note their changes.

The *functional* changes resulting from this change in *form* are far-reaching. Since the levels of all metabolic processes are dependent on, or activated by, the visceral organs, and since the ratio $\frac{\text{visceral-organ weight}}{\text{body weight}}$ declines with increasing body size, the ratio $\frac{\text{functional level}}{\text{body weight}}$ must also, and does, decline with increasing body size.

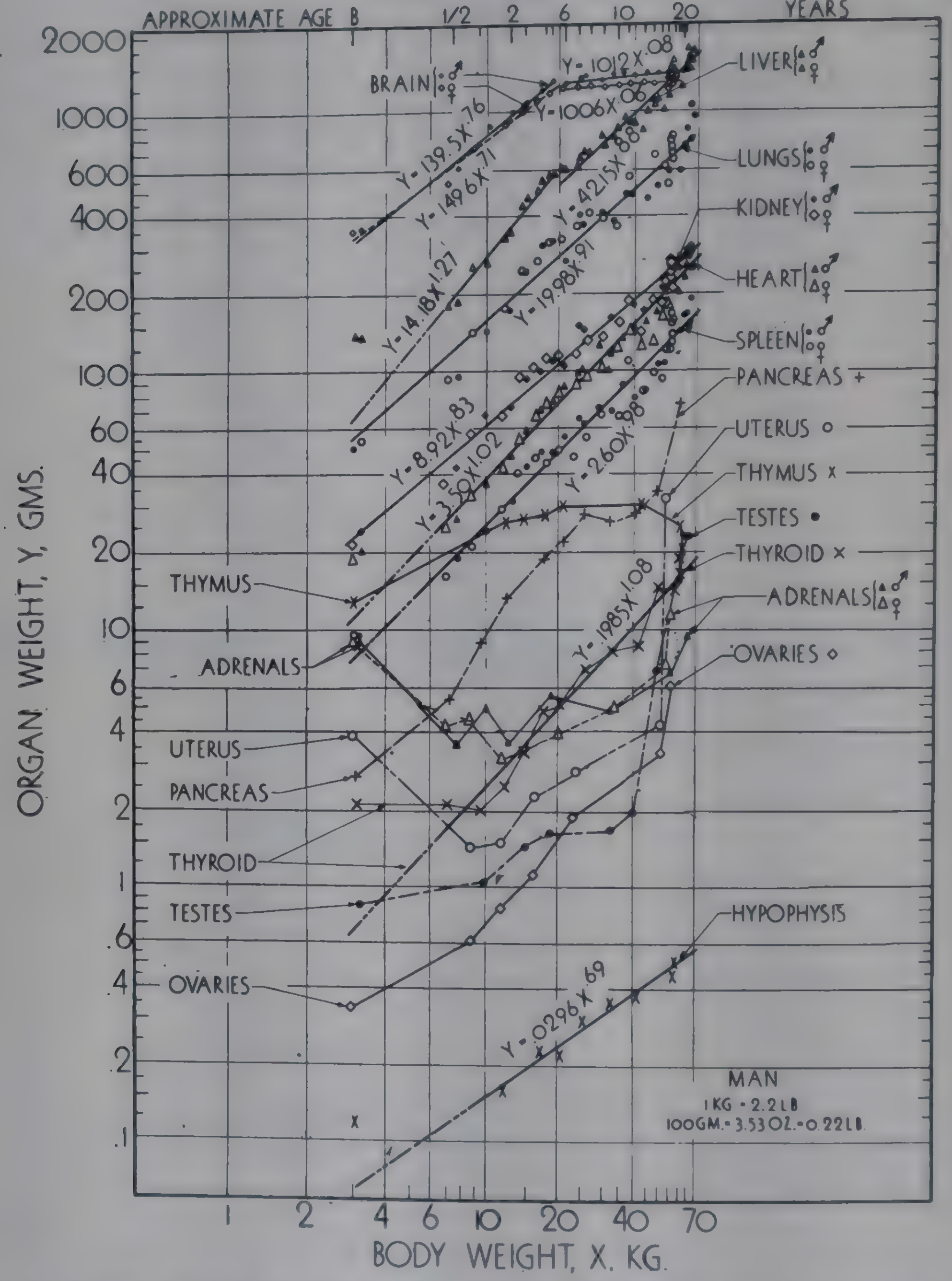

Fig. 17.4. Organ weight as function of body weight plotted on a log-log grid. For sources of data see Edith Boyd: "Outline of physical growth and development" (Burgess, Minneapolis, Minn., 1941). See also Vierordt, H., "Anatamische Daten und Tabellen" and "Tabulae Biologicae."

As a result, most metabolic processes increase not directly with simple body weight, $W^{1.0}$, but with a fractional power of body weight, *i.e.*, the 0.6 to 0.8 power of body weight, or approximately, $W^{0.7}$. This means that increasing body weight by 1 per cent increases the metabolic rate not by 1 per cent but only by 0.7 per cent; the metabolic process increases about 70 per cent as rapidly as body weight. Thus (Ch. 13) the basal energy metabolism of a 100-kg animal is 2070 Cal/day; of a 200-kg animal it is not

4140 Cal/day (twice 2070) but only 3450 Cal/day. While the body increased 100 per cent, from 100 to 200 kg, the metabolism increased $\frac{3450 - 2070}{2070}$ = 68 per cent. Likewise (Chs. 21, 22) we know a 120-lb goat that produced 14 lbs of milk a day but it is probably impossible for a 1200-lb cow to produce 140 lbs of milk a day. A 1200-lb cow may, perhaps, produce 7-fold that of a 120-lb goat, namely 100 lbs of milk a day, but certainly not 10-fold.

This whole discussion adds up to this conclusion: change in size is associated with change in *form* and also with change in *function*. Indeed, function and form are two aspects of the same thing. To be sure, we cannot predict or judge with precision the function from the form, but this is because of our observational limitations; the external features constitute an insignificant aspect of the structure and organization of the body as a whole.

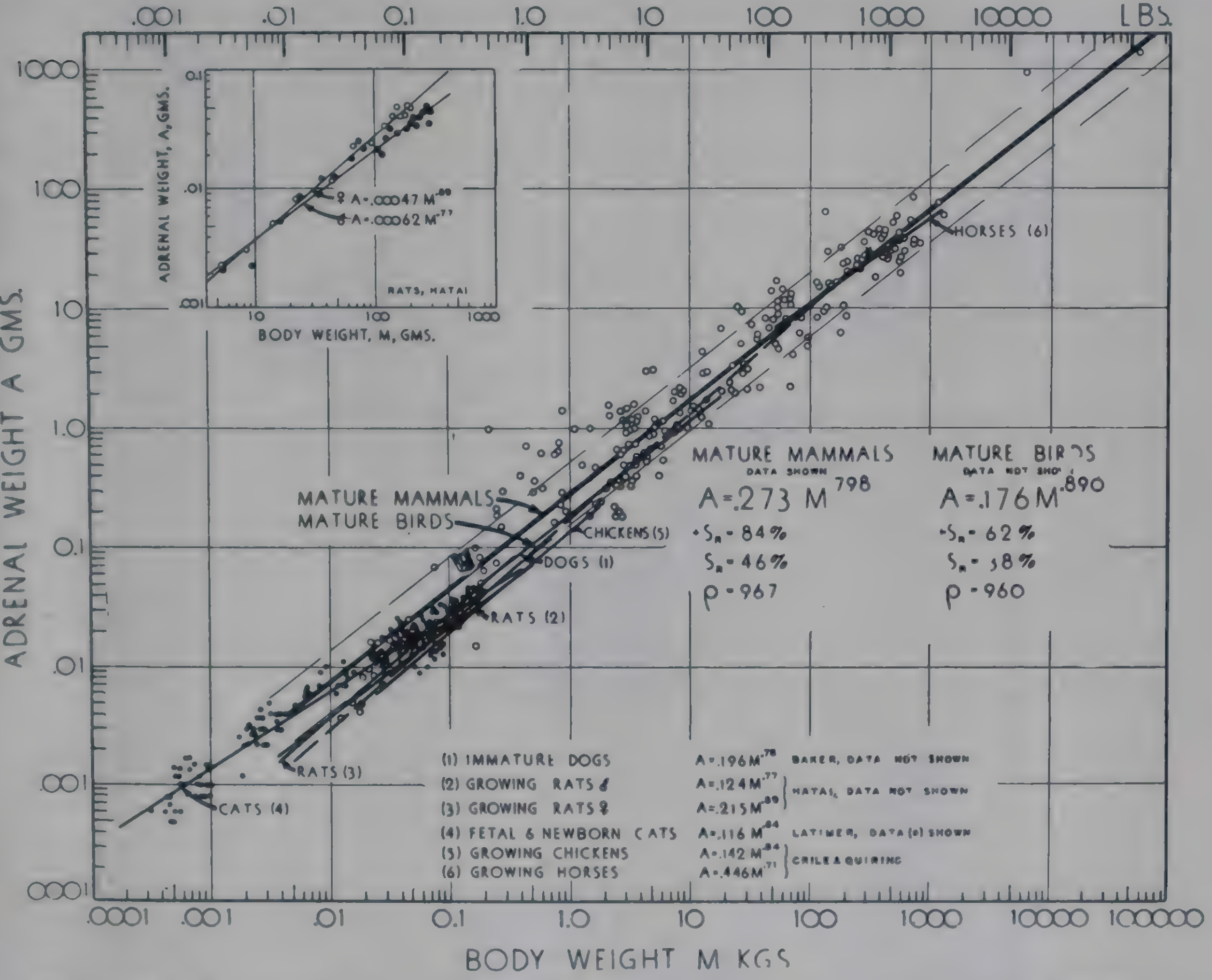

Fig. 17.5a. Supplementing the "atypical" curves (gonads, adrenals) in Fig. 17.4 for man with charts for adrenal weights of animals of different speices (Brody and Kibler).

Summarizing, the necessity for changing the form with increasing size in land animals lies in these geometric facts: (1) weight, which tends to crush the land animal's limbs and which has to be moved by the muscles, varies with the cube of linear size; (2) tensile strength of the muscles and bones which move and support the animal varies with the square of the linear size (cross-section area) of the muscles or bones; (3) surfaces, through which diffusion, nutrition and excretion take place, vary with the square of linear size. Only animals which have evolved a form in harmony with physical or geometric laws on one hand and physiologic needs on the other hand have survived. This situation prompted Lambert and Teissier[5] to remark that while

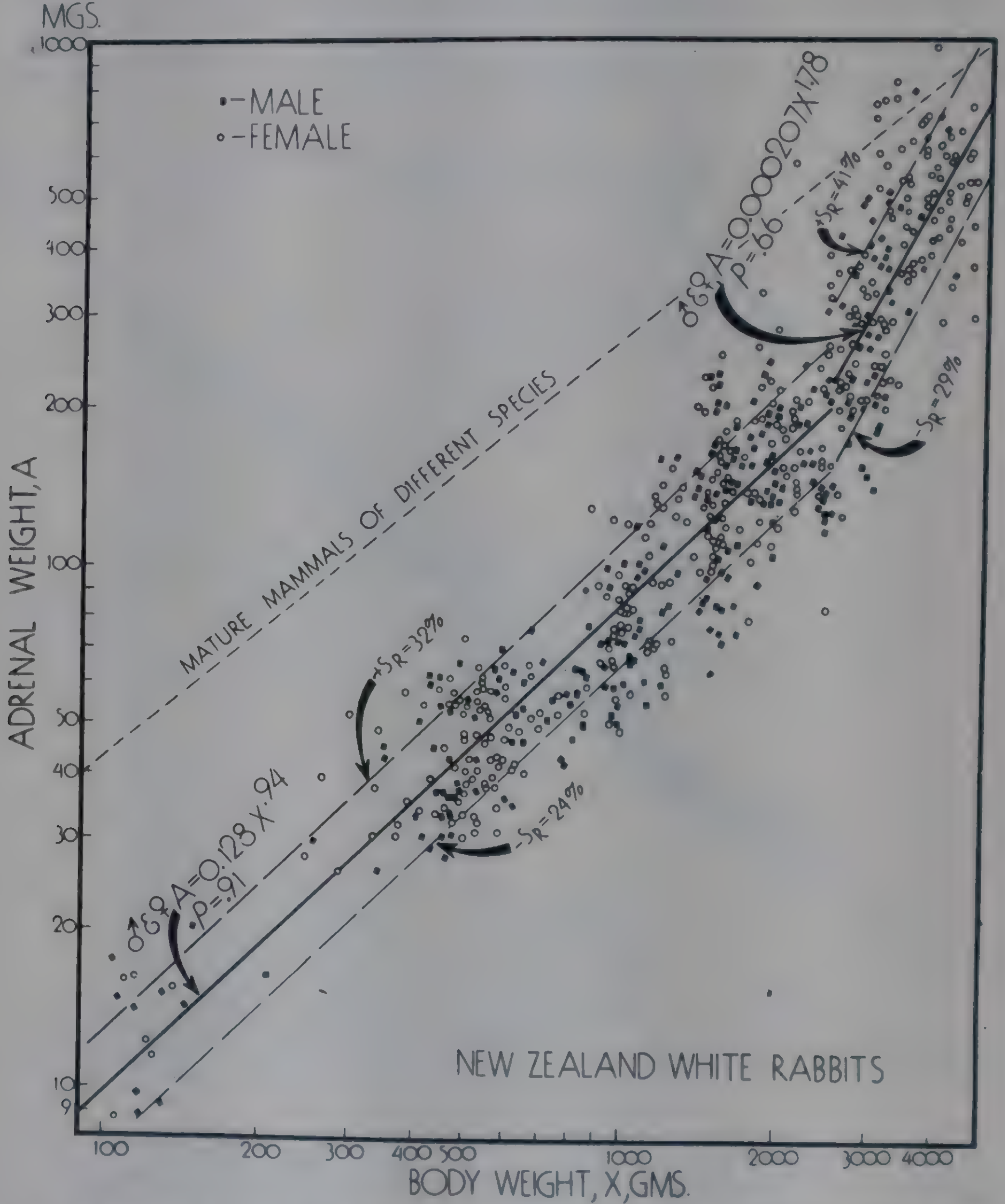

Fig. 17.5b. Adrenal weights of growing rabbits (Kibler, Bergman, and Turner).

physiologists search for a physico-chemical explanation of living phenomena, many physiological laws may be anticipated deductively from geometric and physical interrelations. In fact, about 200 years ago, Galileo, with the aid of his *theory of similitude*, demonstrated that a man cannot build a house, nor nature construct an animal beyond a certain size without changing the form or materials; in other words, large and small organisms cannot remain

[5] Lambert, R., and Teissier, G., "Theorie de la similitude biologique," *Ann. Physiol. et physico-chim. biol.*, #2, p. 22 (1927).

geometrically similar and survive. Aquatic animals are not forced to change much in form with increasing weight because their weight is counterpoised by the displaced water. Changes in form during growth are illustrated in Fig. 17.1a and c.

Differences in body build within the species and breed are, of course, due to special genetic constitutions and to nutritional conditions not explained by the above general principles. Thus persons are classified[6] as fat or pyknic, muscular or athletic, and thin or asthenic. The fat type is characterized by a long digestive tract (25-30 feet of small intestine), whereas the thin type has a short tract (10 to 15 feet of small intestine). There are similar type differences in farm animals, as beef and dairy cattle[7], "dairy" temperament, and so on, and the judging of livestock is mostly judging for type.

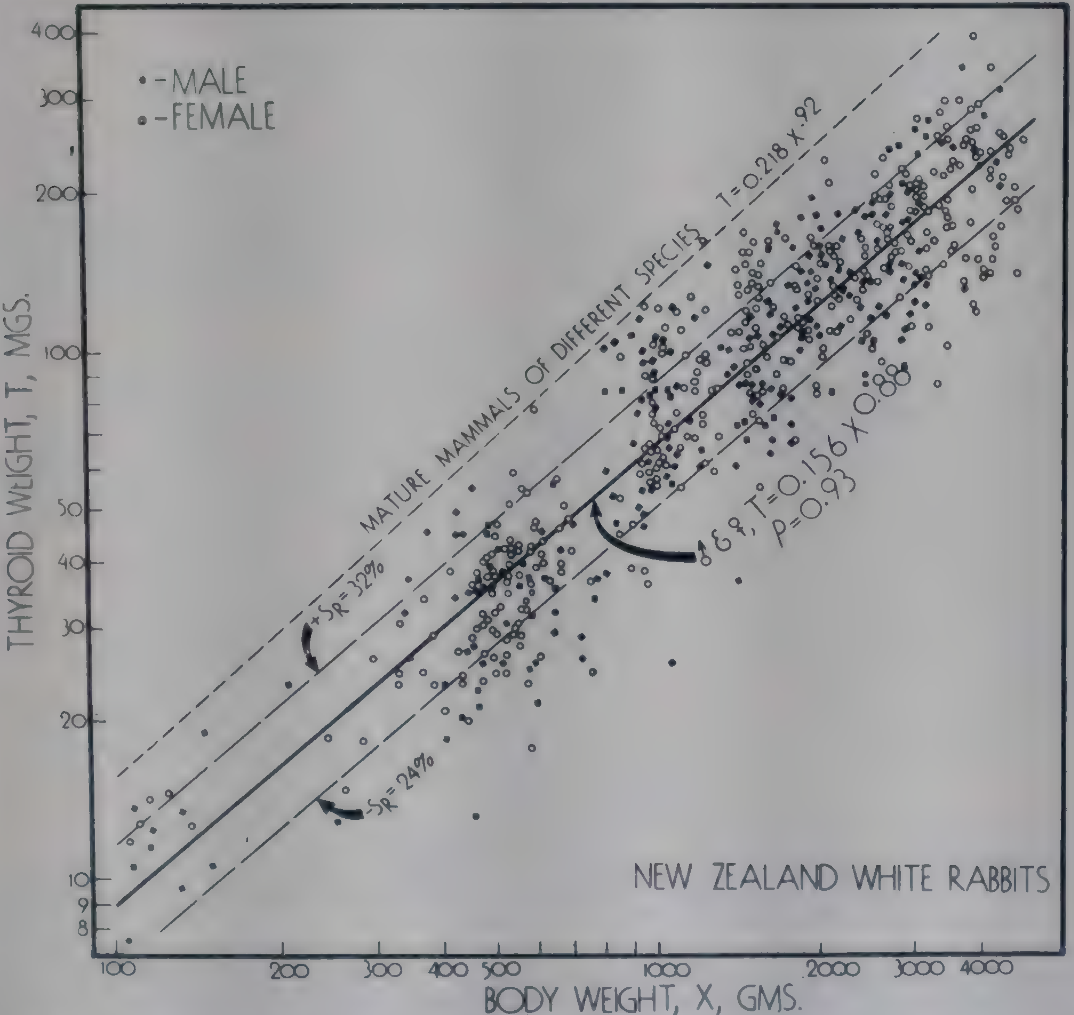

Fig. 17.5c. Thyroid weights of the same growing rabbits as in 17.5b (Kibler, Bergman, and Turner).

Food supply (qualitative, quantitative, and age distribution) exerts a profound influence not only on growth rate and total body weight but also on bodily proportions, "type", and productive capacity. Research on the influence of food supply on type has been pioneered at the Missouri Station[8] and is being pushed vigorously not only in many stations in this country, too many to cite, but especially by the Cambridge (John

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[6] Sheldon, W. H., and Stevens, S. S., and Tucker, W. B., "The varieties of human physique," N. Y., 1940. Kretchmer, E., "Korperbau und Charakter," Berlin, 1921.

[7] Swett, W. W., and Graves, R. R. "Relation between conformation and anatomy of cows," *J. Agr. Res.*, **58,** 199 (1939). See also text books on judging farm livestock, for example, Harrison, E. S., "Judging dairy cattle," Wiley, 1940.

Hammond) School[8,9] (Fig. 17.1c). McCay is investigating this problem especially from the viewpoint of resistance to disease and longevity (Sect. 18.2.4).

One author[10] based his designations of human types as "herbivorous" (fat) and "carnivorous" (thin) on differences in length of the small intestines. Another author[6] designated the fat type as endomorphic or viscerotonic because in this type the digestive viscera, which are derived from the endodermal layer, predominate.

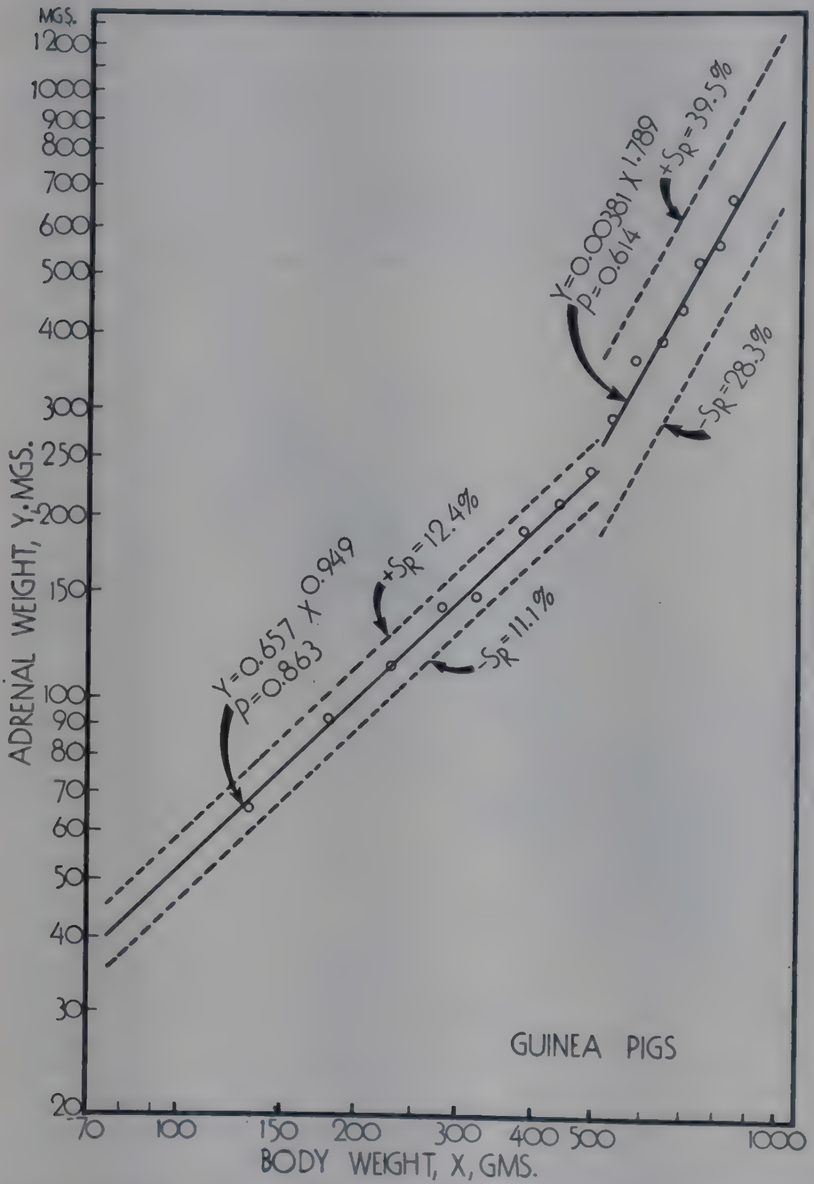

Fig. 17.5d. Adrenal and gonad weights of growing guinea pigs (Mixner, Bergman, and Turner).

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[8] Waters, H. J., "Capacity of animals to grow under adverse conditions," *Proc. Soc. Prom. Agr. Sci.*, p. 78 (1908). Trowbridge, Moulton, C. R., and Haigh L. D., "Limiting food and growth in beef cattle," Univ. Mo. Agr. Exp. Sta. Res. Bull., 30, 1919. Moulton, C. R., "Changes in flesh on underfeeding," *J. Biol. Chem.*, **43,** 67 (1920). Hogan, A. G., "Retarded growth and mature size in beef cattle," Univ. Mo. Agr. Exp. Sta. Res. Bull., 123, 1929.

[9] Hammond, J., "Growth and development of mutton qualities of sheep," London, 1932 (Oliver and Boyd). McMeekan, C. P., "Growth of pig and carcass quality," *J. Agr. Sci.*, Vols. 29–31 (1938–41). Palsson, H., "Meat quality in sheep," *Id.*, Vols. 29–30, 544 and 1 (1939–40). Pomeroy, R. W., *Id.*, **31,** 50 (1941). Hammond and Murray, G. N., "Body proportions of different bacon pigs," *Id.* **27,** 394 (1937). Hirzel, R., "Quality in mutton and beef, proportions of muscle, fat, and bone," *J. Vet. Sci. and Animal Industry*, **12,** 379–550 (1939), and many other papers especially in these two journals. Bonsma, F. N., "Development of lambs," Univ. Pretoria (Pretoria, South Africa), Pub. Series I, Agriculture No. 48, 1939.

[10] Bryant, J., "The carnivorous and herbivorous types of man," *Boston Med. and Surg. J.*, **170,** 795 (1914); **172,** 321 (1915); **173,** 384 (1915).

The fact that some individuals have longer digestive tracts than others should be helpful in dietary adaptation to the respective constitution. Spinach, cabbage and bran may do very well for the "herbivorous" but not the "carnivorous" type, who may need more concentrated victuals.

While a wise physician may recognize a patient's ailment by his "knock on the door", the appearance of his hands[11] or tongue, medical statisticians[12] have computed mathematically the degree of correlation of various ailments to body type, with the result that the fat appear to be inclined to gall bladder and circulatory ailments and to cycloid (manic-depressive) mental disorders; the thin more predisposed to tuberculosis, stomach ulcer, allergies, and to chizoid (schizophrenic) mental disorders. Because of the greater surface area per unit weight in the thin, with corresponding greater exposure of nerve endings to the surroundings, the thin is likely to be more sensitive, irritable, high strung and introvert than the fat, who is likely to be easy going, cheerful and extrovert.

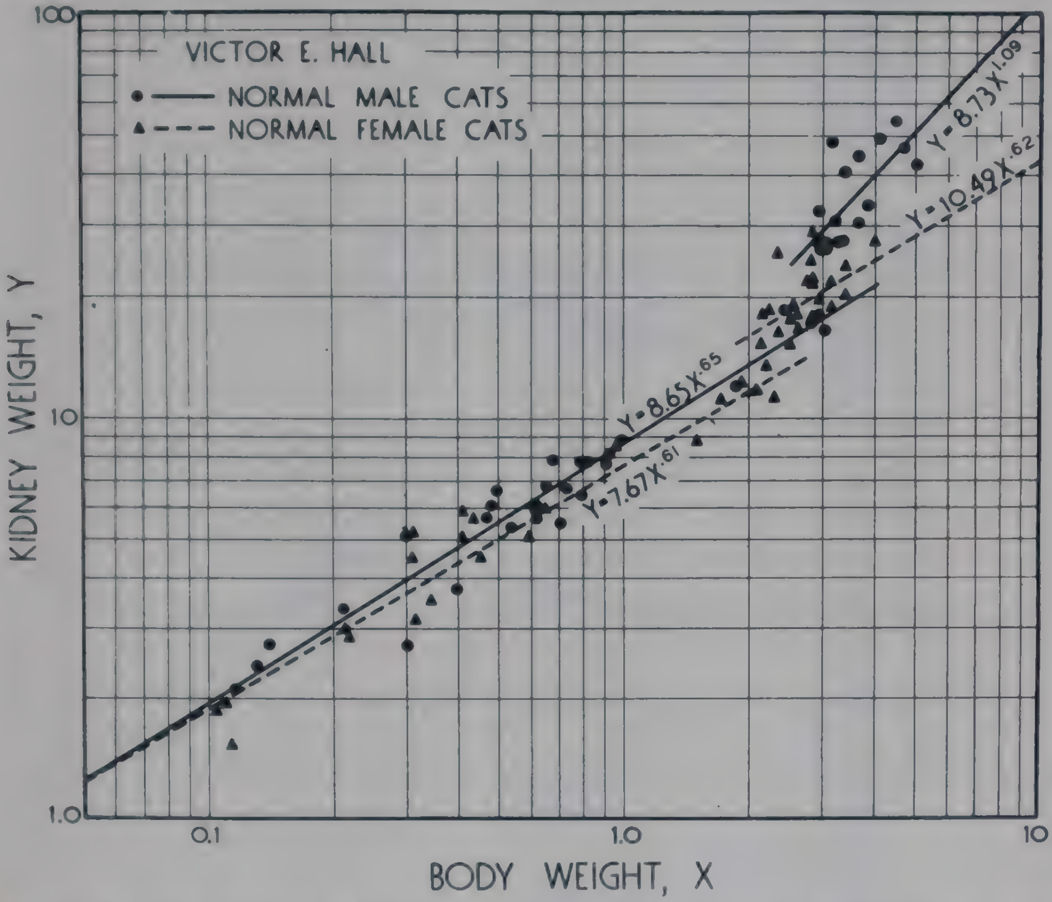

Fig. 17.5e. Kidney weight of growing cats (Brody, plotted from unpublished data by Hall) showing an apparent "break" paralleling the adrenal "break." (Cf. p. 625.)

The endocrine background is likely to differ in the various types (Ch. 7). It is generally known that the basal metabolism tends to be higher in the muscular and the tall-thin, than in the fat, which may reflect greater thyroid activity in the muscular and tall-thin than in the fat. On the other hand, the fat tend to be hypopituitary and hypogonadal (Frohlich syndrome) and the muscular tend to be hyperpituitary (acromegaly).

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[11] Wolff, Charlotte, "The human hand," Knopf, 1943.

[12] Pearl, R., "Constitution and health," London (Kegan Paul), 1933. Petersen W. F., "Constitution and disease," *Physiol. Rev.*, **12**, 283 (1932). Pearl, R., "The research for longevity," *Sci. Monthly*, **46**, 462 (1938). Wertheiner, F. I., and Hesketh, F. E., "The significance of the physical constitution in mental disease," *Med. Monogr.*, **10**, Baltimore (1926). Ciocco, A., "The historical background of the modern study of constitution," *Bull. Inst. Hist. Med.*, **4**, 23 (1936).

17.2: Notes on dimensional analysis.[13] The method of dimensional analysis is comparable in simplicity, power, and generality to that of thermodynamics. The method of dimensional analysis, being geometric in nature, is not concerned with detailed mechanisms, but, like certain aspects of thermodynamics, it expresses statistical results of certain interactions. Thus power functions such as the one discussed in Chapter 13, concerned with the relation between metabolism and body weight, or such as will be discussed in a later section of this chapter, may be derived analytically and *independently of detailed physiologic or biologic considerations*. Thus energy-producing (as

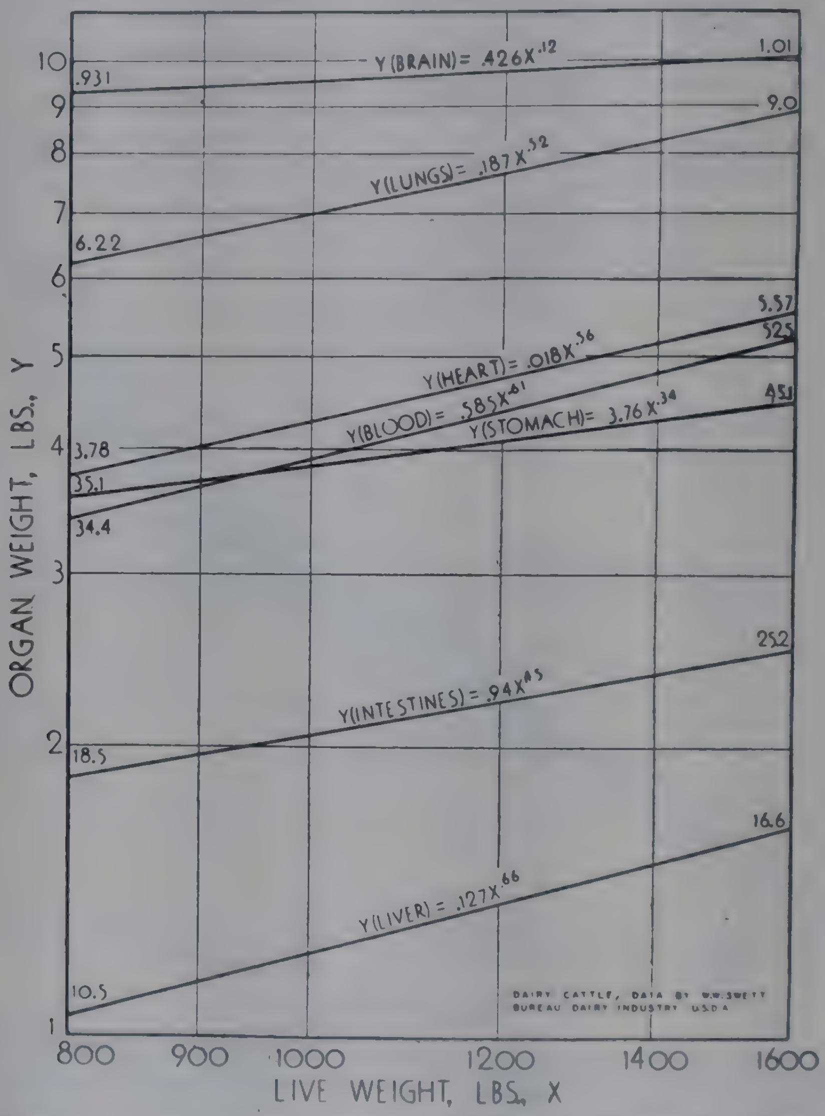

Fig. 17.6. The relation of organ weights to body weight in mature cattle. The curves represent the equation $Y = aX^b$ fitted by the method of least squares to data kindly furnished by W. W. Swett, Bureau of Dairy Husbandry, U. S. Dept. of Agriculture. For description of animals see Swett, W. W., and Graves, R. R., *J. Agr. Res.*, **58**, 199 (1939). The numerical values at the beginning and end of curves represent the organ weight in pounds for 800 and 1600 pound cattle.

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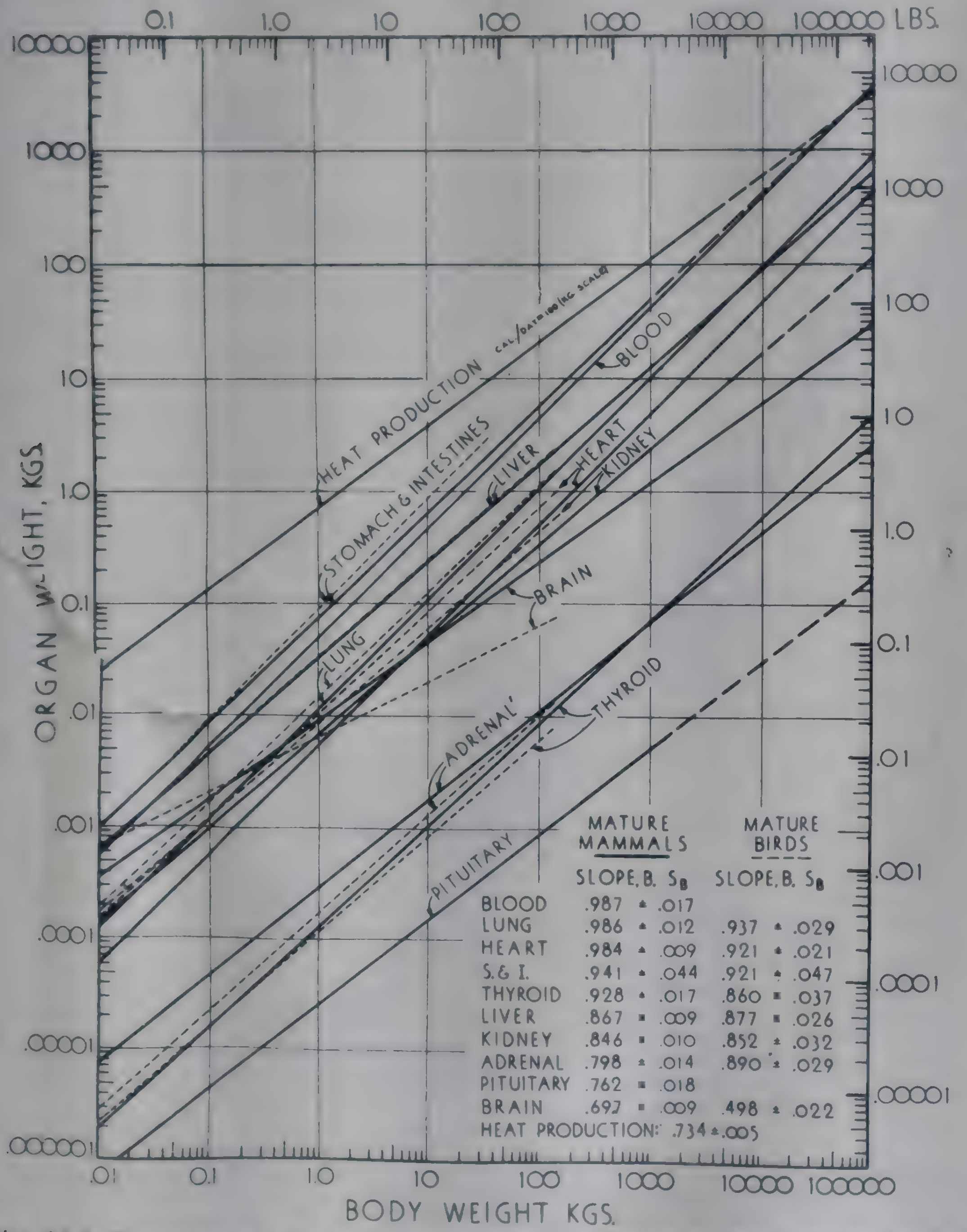
[13] See D'A. W. Thompson[2]; Tolman, R. C., "The principle of similitude and the principle of dimensional homogeneity," *Physical Rev.*, **6**, 219 (1915); **9**, 237 (1917). Lambert, R., and Teissier, G., "Theorie de la similitude biologique," *Ann. Physiol. et physicochim. biol.*, **3**, 212 (1927); Teissier, G., "La grandeur de métabolisme en fonction de la taille. Étude de biometrie théorique," *Id.* **4**, 1 (1928).

sal metabolism'') properties vary with the square of the linear dimensions, regardless hether the body is an animal or a steam engine, while the weight of the body, animal ngine varies with the cube of the linear dimensions; hence from dimensional analysis, heat production or available long-range energy will tend to vary with the $\frac{2}{3}$ power of weight of the animal or engine.



	MATURE MAMMALS		MATURE BIRDS	
	SLOPE, B.	S_B	SLOPE, B.	S_B
BLOOD	.987	± .017		
LUNG	.986	± .012	.937	± .029
HEART	.984	± .009	.921	± .021
S. & I.	.941	± .044	.921	± .047
THYROID	.928	± .017	.860	± .037
LIVER	.867	± .009	.877	± .026
KIDNEY	.846	± .010	.852	± .032
ADRENAL	.798	± .014	.890	± .029
PITUITARY	.762	± .018		
BRAIN	.697	± .009	.498	± .022

HEAT PRODUCTION: .734 ± .005

Fig. 17.7. Summary of the curves representing the relation of organ weight to body weight of mature mammals (heavy lines) and birds (light broken lines) of different species. The numerical values of the slopes (b in the equation $Y = aX^b$) and of the standard error, S_b, of the slopes, b, are given for each curve. The low values of S_b ndicate a high degree of stability for these slopes, especially for the mammals.

This derivation is independent of the fact that the body is living. The "surface law", relating basal metabolism to surface area, on the other hand, is derived not from general physical or geometric laws, but from the biologic consideration that in the course of evolution only those animals survive whose rate of heat production balances their rate of heat dissipation, which is proportional to surface area (square of linear

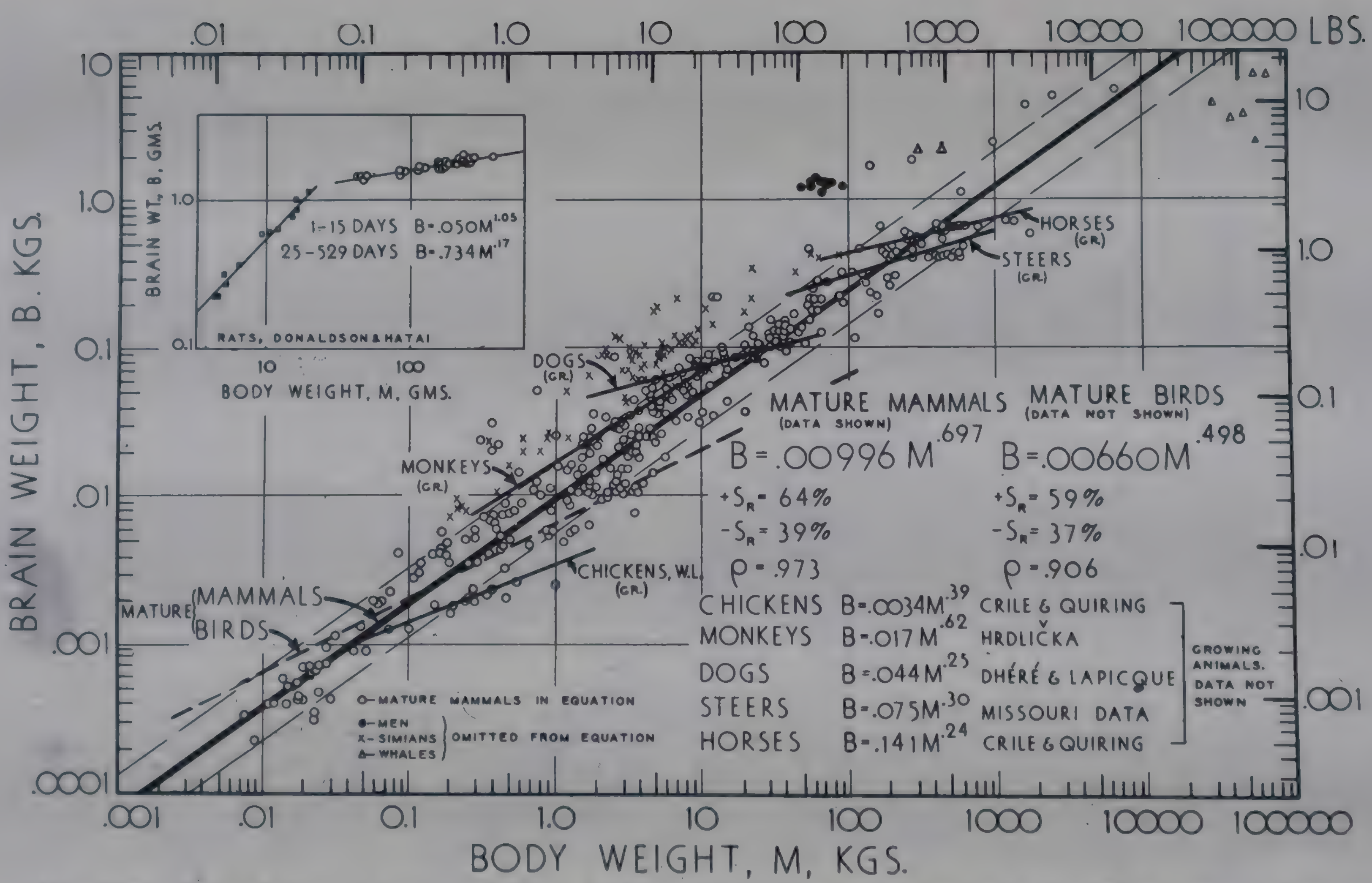


Fig. 17.8a. The relation of brain weight to body weight plotted on a log-log grid. The given data points are for *mature mammals* only. The heavy continuous line represents the equation $Y = aX^b$ fitted, by the methods of least squares, to mature mammals of different species. The broken curve similarly represents mature birds; the other curves (GR) represent the indicated animals in various stages of growth. The five broken lines represent the standard error of estimate, Sr, including between them $\frac{2}{3}$ of the data points. The letter rho represents the index of correlation, corresponding to the coefficient of correlation for linear equations. All charts follow the same system.

dimensions). Dimensional analyses also lead to the conclusion that while a linear equation relating metabolism to body weight may be practically as satisfactory, it is less rational than a power(logarithmic or parabolic) equation.

According to dimensional analysis, metabolism varies with the $\frac{2}{3}$ power of weight in geometrically similar figures. Actually metabolism does not vary with the $\frac{2}{3}$ power of weight, because the large animal is not geometrically similar to the small, due to change in form and substance during growth, as might be expected, again, from dimensional analysis and the principle of similitude. The method of dimensional analysis thus predicts that metabolism should vary with a fractional power of weight, close to the $\frac{2}{3}$ power of weight, but not exactly with the $\frac{2}{3}$ power of weight. It has been suggested that the weights of certain visceral organs should, like surface area, vary with the square of the linear dimensions[14] and that excitation[15] should also vary with area (of the excitable elements).

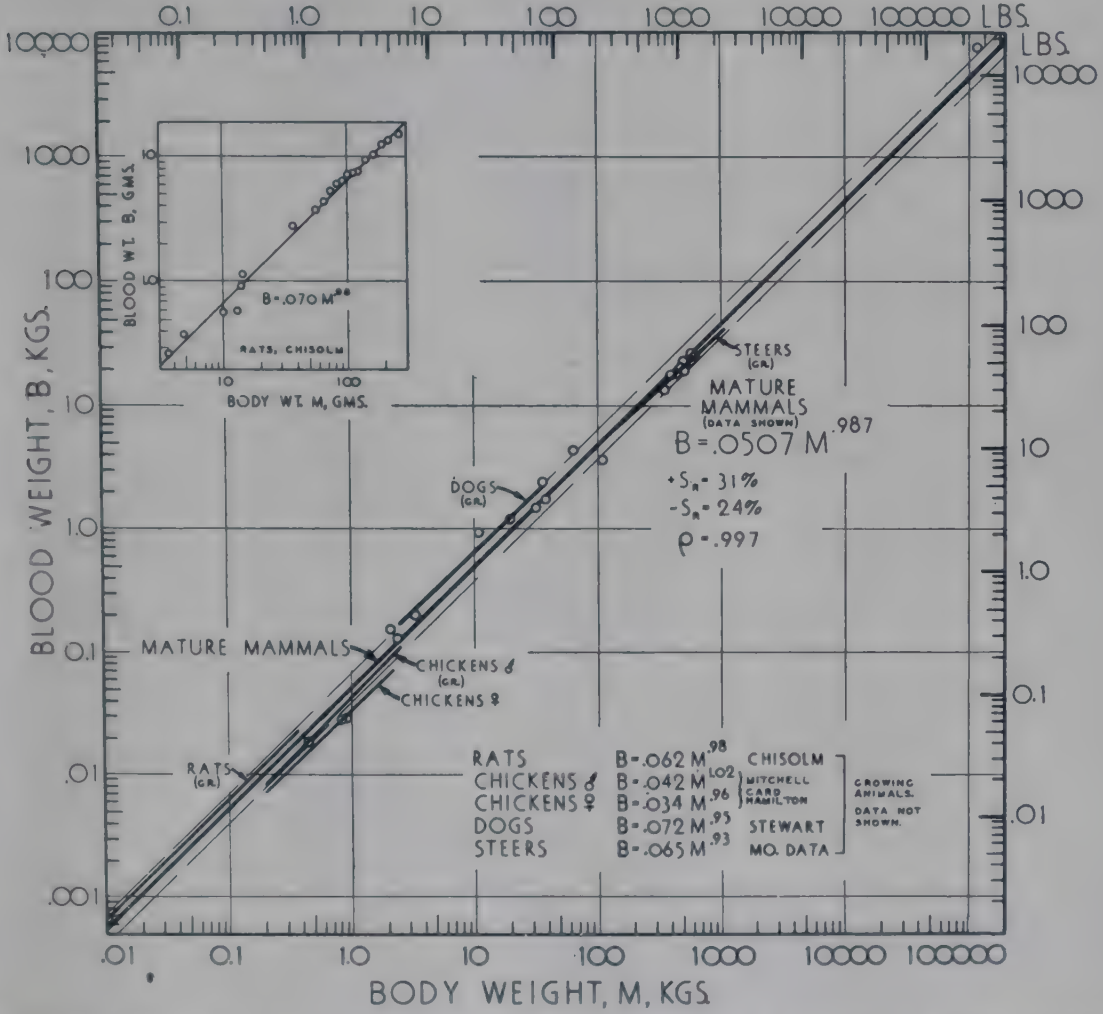


Fig. 17.8b. Blood weight, unlike brain weight, shows a virtually linear relation to body weight and slight species differences. The heart (Fig. 17.10) also tends to vary linearly.

The method of dimensional analysis is said to have been formulated by Fourier and also by Galileo. The method (1) postulates that many quantities (see the following table) are derivable from a few fundamental quantities or dimensions, and (2) specifies that the dimensions on the two sides of a physical equation must be homogeneous and balanced. Skill in the use of dimensional analysis involves familiarity with the fundamental and derived quantities or dimensions and definitions, and facility in algebraic technique.

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[14] Brandt, A., "Das Hirngewicht und die Zahl der peripherischen Nervenfasern in ihrer Beziehung zur Körpergrösse," *Biol. cent.* **18**, 475 (1898). Du Bois, E. "Sur le rapport du poids de l'encephale avec la grandeur du corps chez les Mammiferes," *Bull. Soc. Anthrop.*, **8**, 337 (1897).

[15] *Cf.* Crozier, W. J., and Holway, A. H., "Theory and measurement of visual mechanisms," *J. Gen. Physiol.*, **23**, 101 (1939).

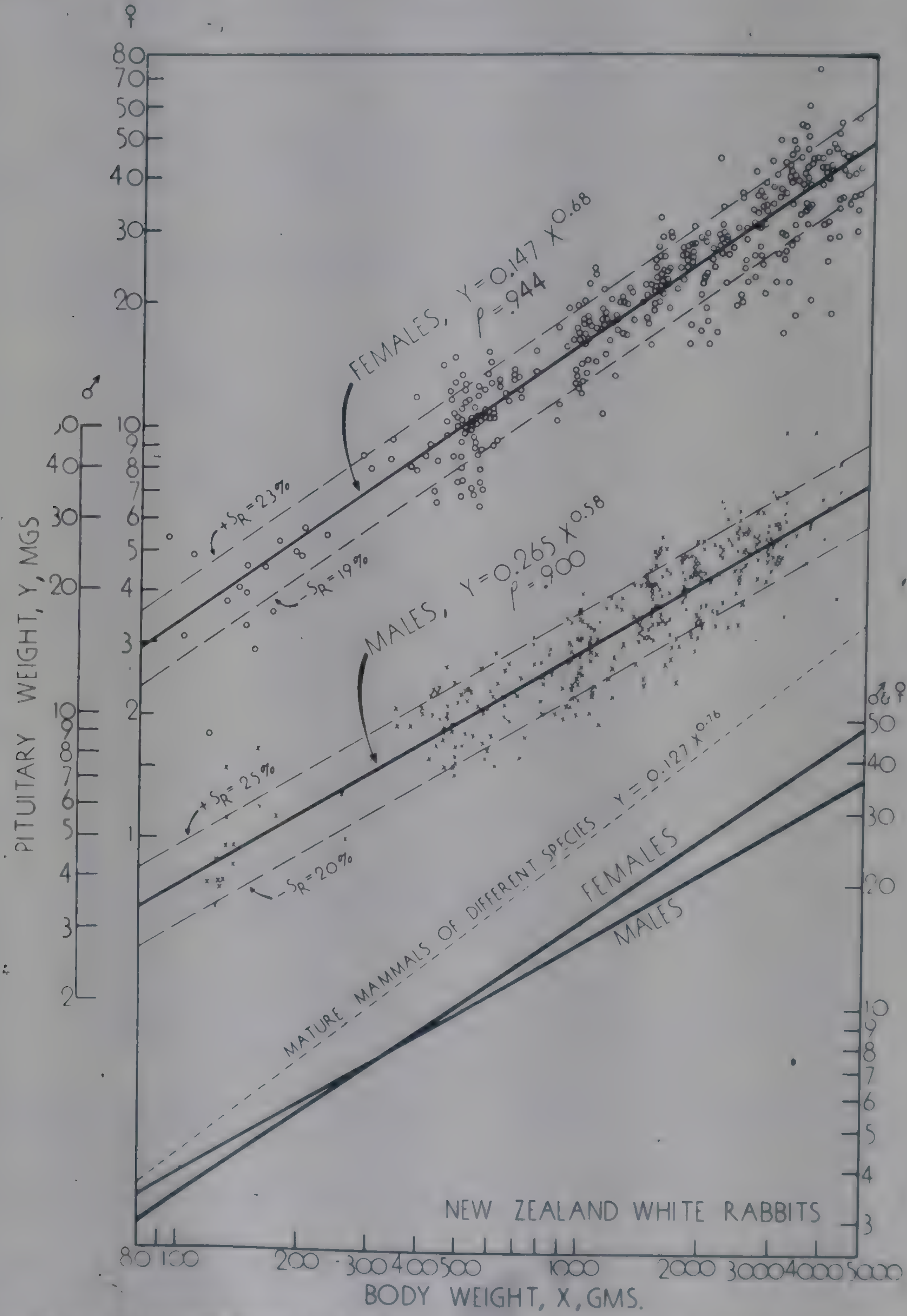

Fig. 17.9a. Pituitary weight of different species (Brody and Kibler, Mo. Agr. Exp. Sta. Res. Bull. 328), and of rabbits (Kibler, Bergman, and Turner).

There are several—there were formerly three but they were increased by Tolman to

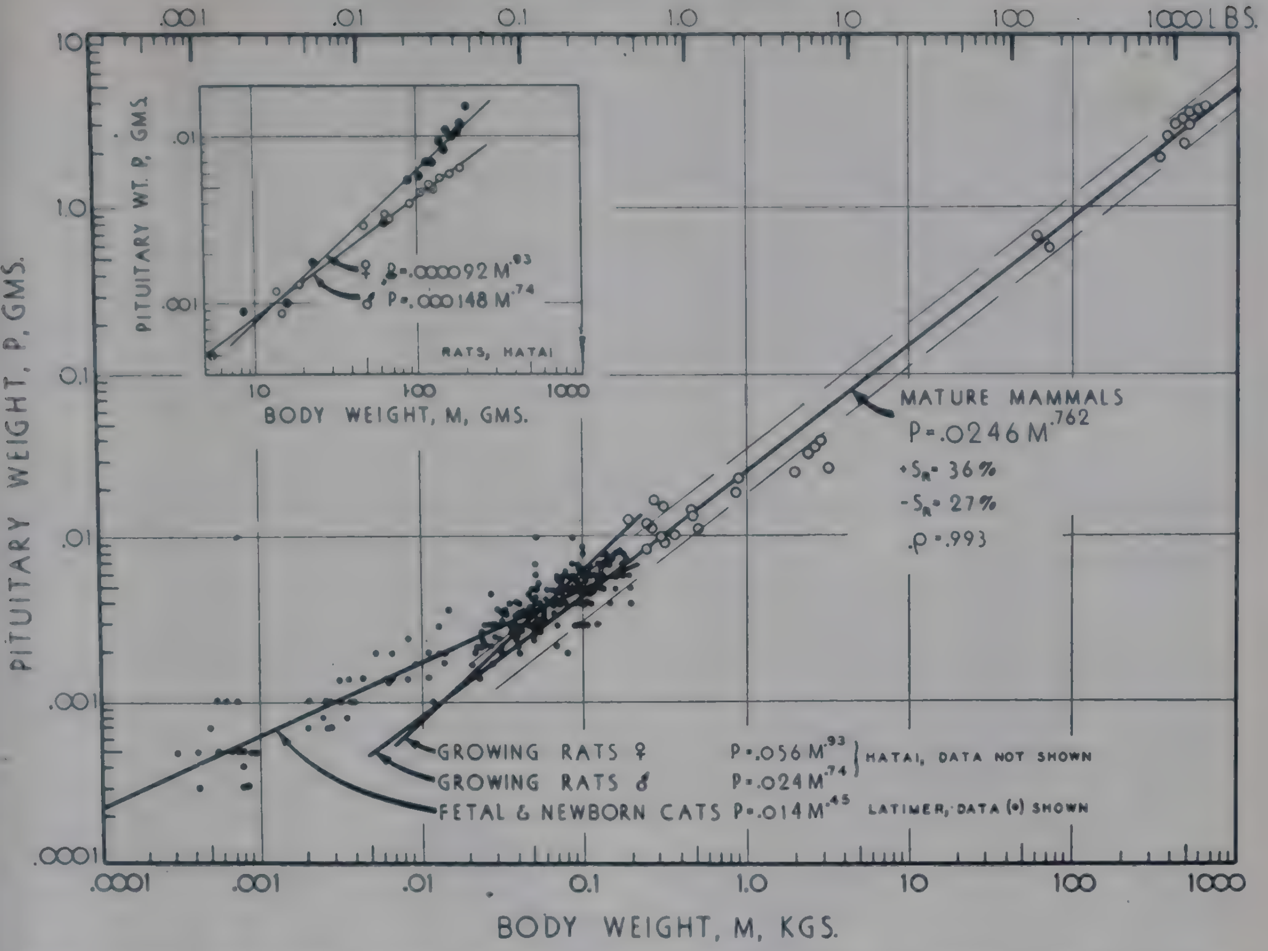

Fig. 17.9b. Pituitary weight of different species (Brody and Kibler, Mo. Agr. Exp. Sta. Res. Bull. 328), and of growing rats (insert).

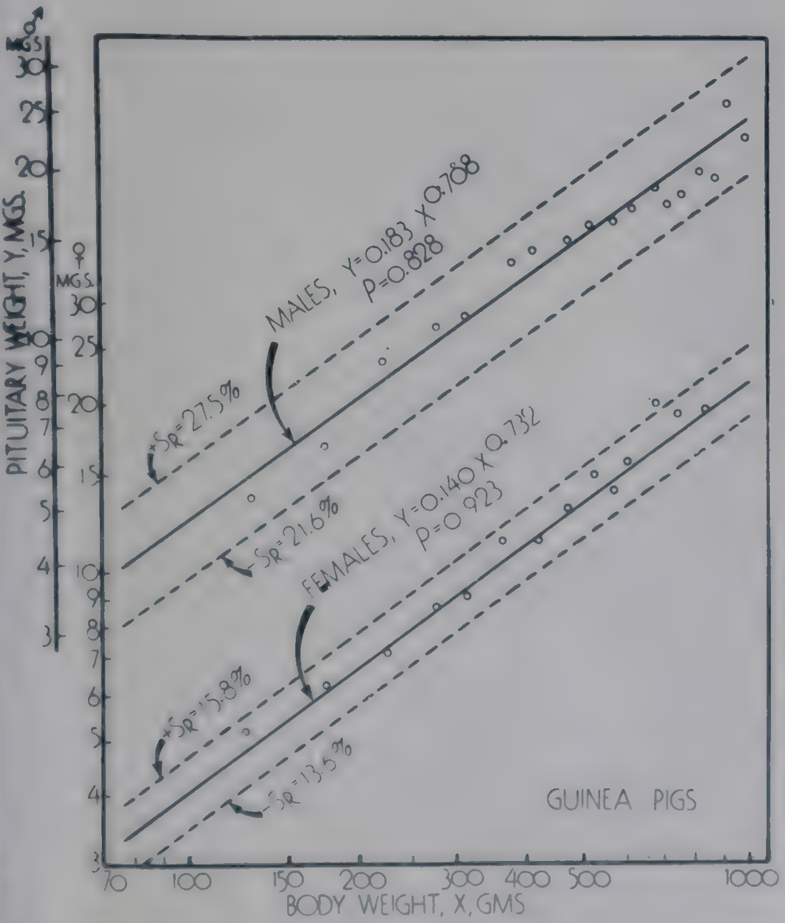

Fig. 17.9c. Pituitary weight of guinea pigs [Mixner, Bergman, and Turner, *Endocrinology*, **31**, 59 (1942)].

five—fundamental dimension or quantities, namely (1) length, l, fundamental for spatial quantities; (2) time, t, for temporal quantities; (3) mass, m, for mechanical quantities; (4) electric charge, e, for electrical quantities; (5) entropy, or degree of "run-downess", S, for thermodynamic quantities.

Other kinds of quantity may be derived in terms of these five fundamentals. Thus it is customary to regard a quantity of velocity, v, as a quantity of length, l, divided by quantity of time, t; a quantity of volume, v, as the product of three quantities of length; a quantity of density, d, as a quantity of mass, m, divided by a quantity of volume, and so on.

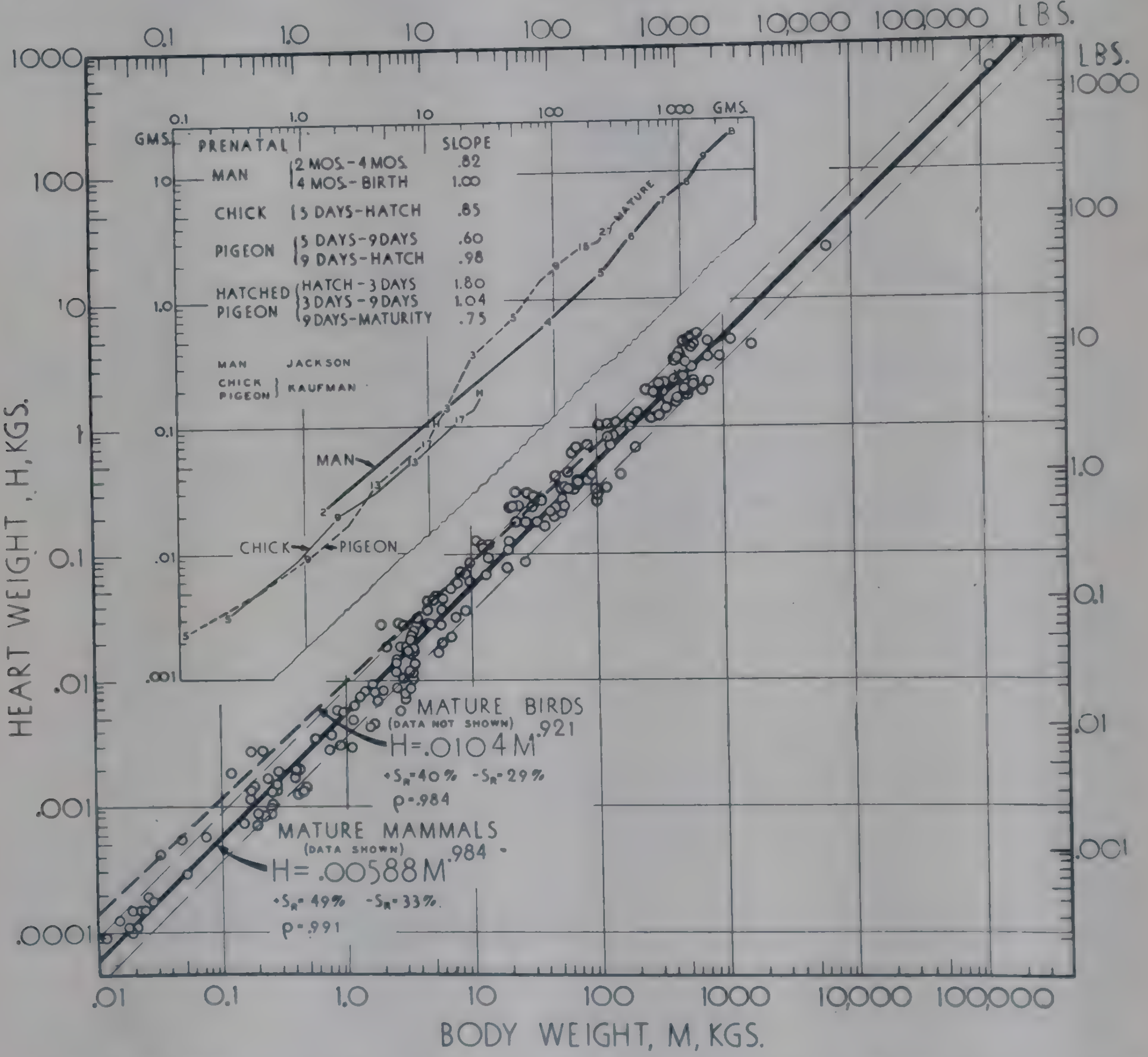

Fig 17.10a. Heart weight vs. body weight during prenatal growth (insert upper left) and in mature animals of different species. Note that the "athletic" land animals have relatively larger hearts than the non-athletic and marine animals.

Velocity is said to have the dimensional formula of length divided by time, symbolized by the formula, lt^{-1} (or l/t); likewise, momentum, which is quantity of mass, m, multiplied by a quantity of velocity, lt^{-1}, is said to have the dimensional formula mlt^{-1}. The dimensional formula is a shorthand statement of the definition of that kind of quantity in terms of quantity chosen as fundamental, and hence is also a partial statement of the physical nature of the quantity in question.

The following table illustrates the above discussion.

SPATIAL OR GEOMETRIC QUANTITIES

	Symbol	Dimension
Length	l	l
Area	A	l^2
Volume	V	l^3

TEMPORAL OR KINEMATIC QUANTITIES

	Symbol	Dimension
Time	t	t
Velocity, linear speed	v	lt^{-1}
Acceleration	a	lt^{-2}
Frequency, revolutions per unit time		t^{-1}

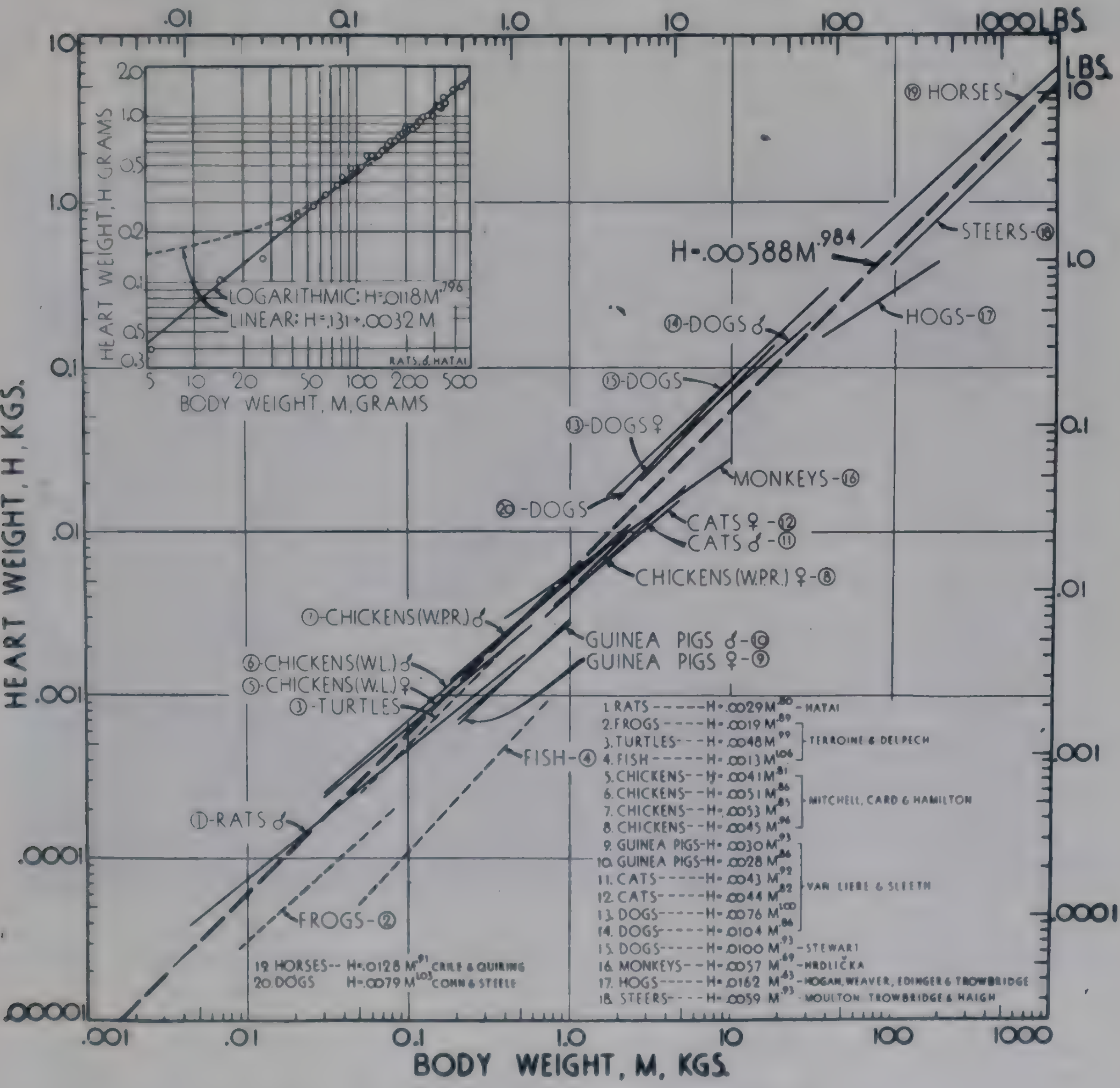

Fig. 17.10b. See legend for Fig. 17.10a.

There are, similarly, mechanical, thermodynamic, and electrical quantities.

The following simple dimensionally homogeneous equations were previously discussed (Ch. 13) in connection with the area problem.

The equation

$$A = V^{1/3}l$$

(Note: A = surface area, V = volume, l = linear size) is dimensionally

$$l^2 = l^{3/3}l = l^2$$

The equation

$$A = V^{1/2}l^{1/2}$$

is dimensionally

$$l^2 = l^{3\times1/2}l^{1/2} = l^2$$

The equation

$$A = V^{.425}l^{.725}$$

is dimensionally

$$l^2 = l^{3/3\times.425}l^{.725} = l^{1.275}l^{.725} = l^2$$

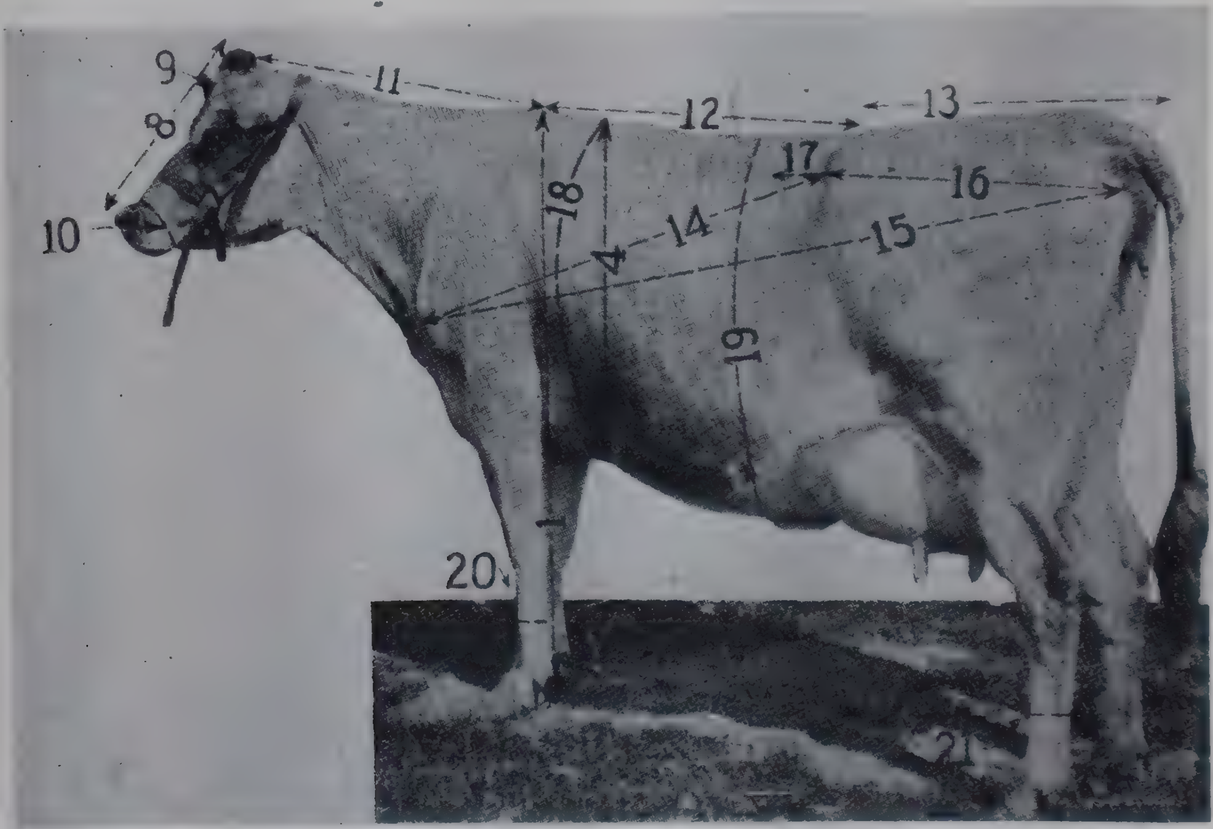

Fig. 17.11. Linear measurements taken of dairy cattle, described in Table 17.7, page 650, and referred to in Figs. 17.12a and b. For measuring methods see Figs. 16.62a to d (pp. 560–563).

From the above and other dimension equivalents, it may be shown that in bodies geometrically, chemically, physically, and environmentally similar, heat production should vary with the square of linear size; likewise, in similar animals under similar conditions, heat production should vary inversely with the squares of the pulse rate or respiration rate (heart rate and respiration rate, being frequencies, have the dimension of $1/t$ or t^{-1}) or directly in proportion to the amount of blood supply (which is the product of pulse rate and volume of blood, having the dimension of l^2); or what is the same, the heat production *per unit weight* should vary inversely with the cube root of weight ($Q/W = aW^{\frac{1}{3}}$, which is the same as $Q = aW^{\frac{2}{3}}$) or directly with the pulse rate or respiration rate (Sect. 24.5.4).

17.3: Equations relating part to whole. The method of dimensional analysis is strictly applicable only to bodies which are similar in space and time, such as small and large spheres. Since small and large animals—infants and adults, for example—are not similar in space and time, this method is useful for rough approximations only. An empirical—less logical—approach is more inviting at this time.

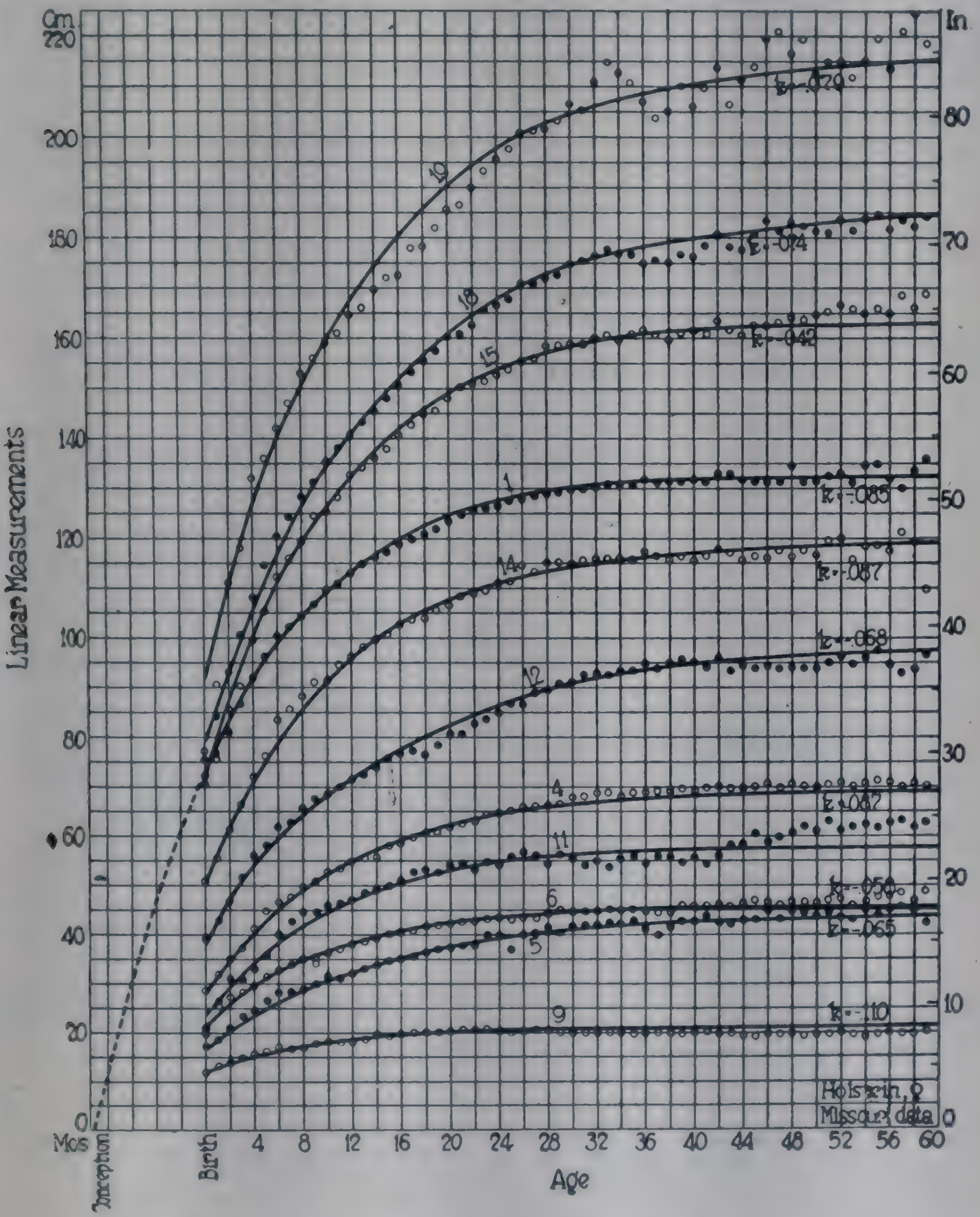

Fig. 17.12a. Age course of linearly measured complexes (Fig. 17.11). The continuous curves represent the equation $Y = A - Be^{-kt}$ fitted to the data. For the value of the constants see Table 17.7.

Common-sense considerations and experience, especially in chemistry, physics, and engineering, and even in economics, indicate that the *percentage change* in one variable tends to vary directly with the *percentage change* in a related variable. As percentage change is the same as logarithmic change, one may say that the logarithmic change in one variable tends to vary directly with the logarithmic change in a related variable. A logarithmic equation has the same meaning as a parabola, a hyperbola, or a power equation, though it has a different form. To illustrate, it was shown (introductory section to this chapter, and Chapter 13) that surface area, S, varies with the ⅔ power of volume or weight

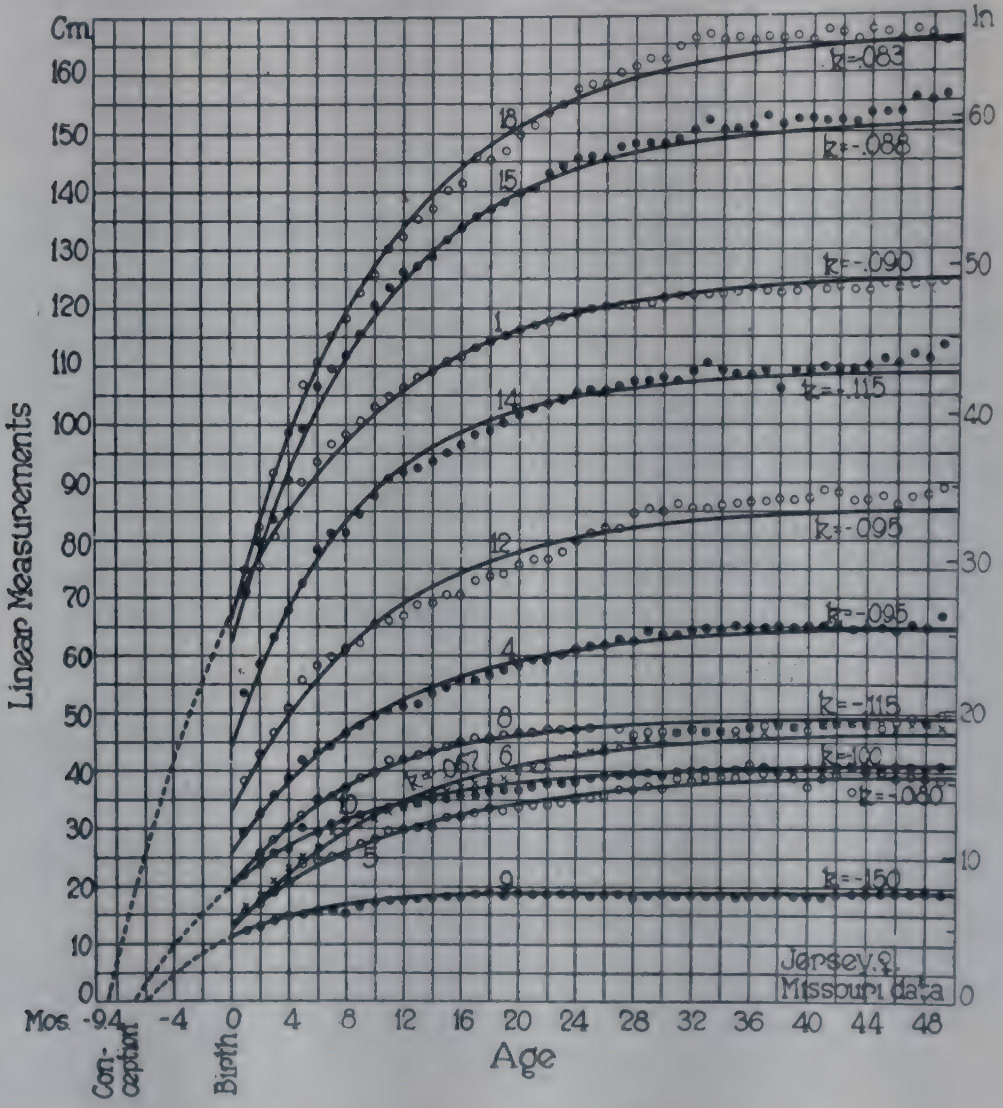

Fig. 17.12b. See legend for Fig. 17.12a.

$$S = aW^{\frac{2}{3}} \tag{1}$$

which is the power-equation or parabola form; in the straight-line logarithmic form it is

$$\log S = \log a + \tfrac{2}{3} \log W \tag{2}$$

Equations (1) and (2) represent the same thing in different forms. Usually equations (1) and (2) are written

$$Y = aX^b \tag{17.3}$$

and in terms of logarithms, which gives a linear form, it is

$$\log Y = \log a + b \log X \tag{17.4}$$

similar to the familiar linear equation

$$Y = a + bX$$

The exponent, b, which has the value ⅔ or 0.67 for the area-weight relation, is the ratio of the percentage change in Y to the corresponding percentage change in X; b is the slope of $\log Y$ plotted against $\log X$. For the area-weight relation, the percentage increase in surface area is ⅔ that of the percentage increase in weight.

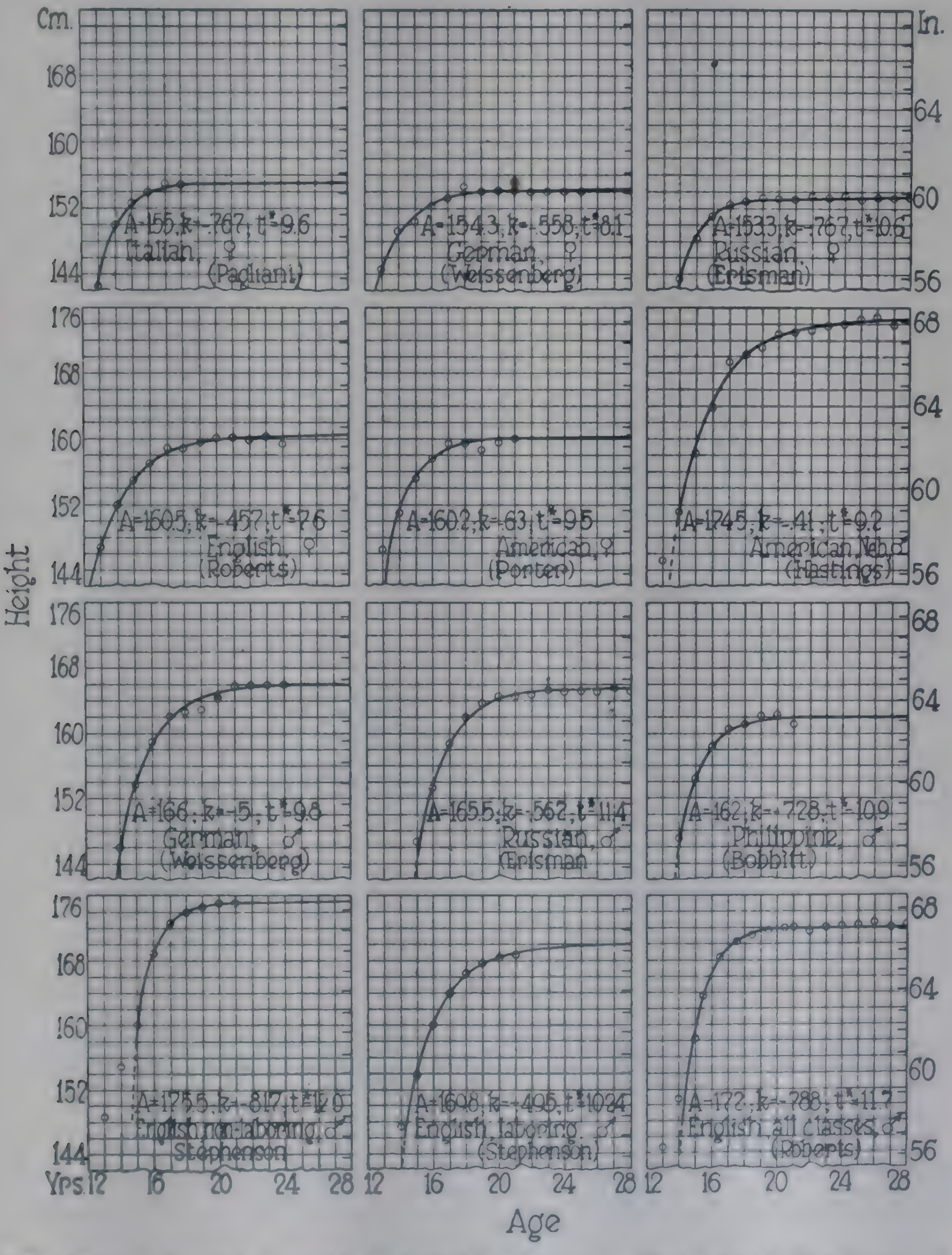

Fig. 17.13. Postpubertal growth in height of man. Note that the average mature height ranges from less than five to nearly six feet; yet all curves follow the course represented by the equation $Y = A - Be^{-kt}$. (The values of k and t^* are with respect to age in *years* for humans as contrasted to *months* for cattle.)

Likewise (Ch. 13) the basal metabolism, Y, varies with weight, X,

$$Y = aX^{0.73}$$

or

$$\log Y = \log a + 0.73 \log X$$

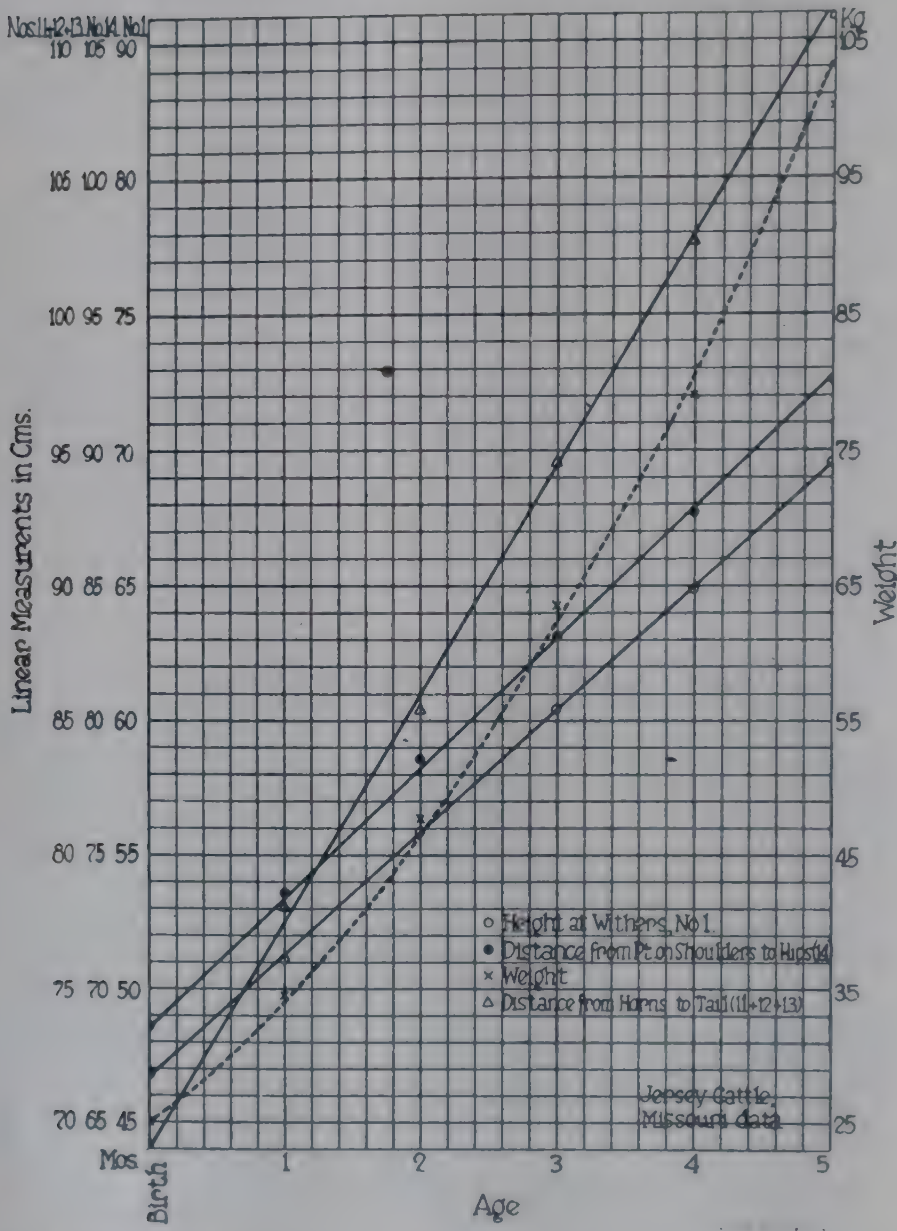

Fig. 17.14a. Prepubertal growth in cattle proceeds at a constant *percentage* rate for weight (broken curve), and at a constant *time* rate for linear growth (smooth curves).

meaning that the percentage increase in metabolism, Y, is 0.73 time the percentage increase in body weight, X; or increasing body weight, X, 1 per cent increases metabolism, Y, 0.73 per cent.

The method of fitting this equation to data is elementary and uninteresting, and has been described in detail in Chapter 13. The historic aspect is, on the contrary, interesting and entertaining. About half a century ago, Snell[16], DuBois[17], and Lapicque[18] wondered how brain size of different species should be compared in such a way as to demonstrate clearly that man's brain is proportionately larger than the brain of other species. They had no doubt that man's brain is relatively larger, although numerical comparisons gave ambiguous results. Thus comparison of absolute size (pounds, grams)

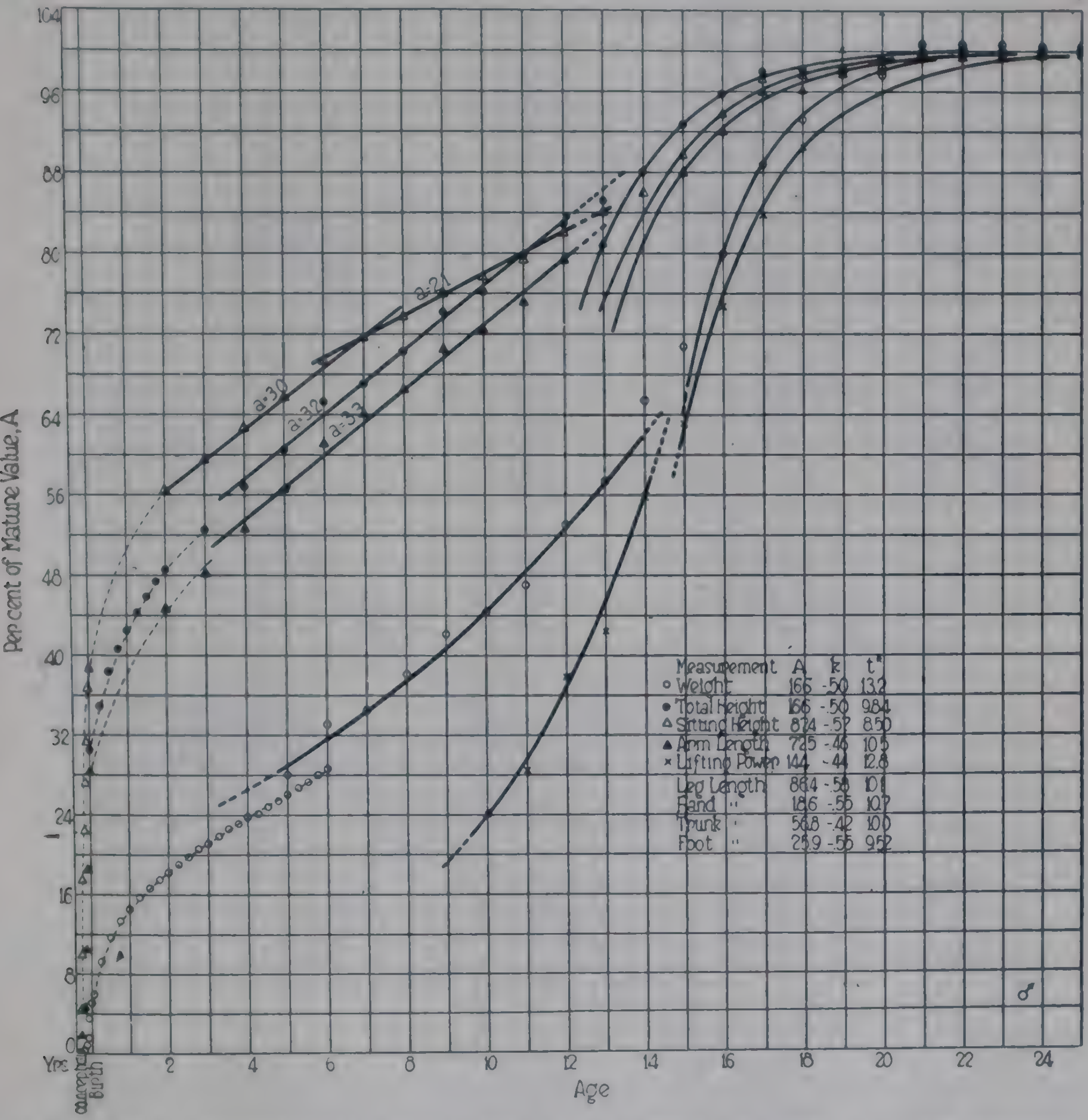

Fig. 17.14b. Postpubertal weight and linear growth in man decline exponentially ($Y = A - Be^{-kt}$); prepubertal weight growth in man increases exponentially ($Y = Ae^{kt}$) and linear growth, linearly ($Y = aX + b$). (Data from S. Weissenberg, "Das Wachstum des Menschen nach Alter, Geschlecht und Rasse," Stuttgart, 1911).

of brain indicated that elephants had larger brains; comparison of size per unit body weight, that is, comparison of the ratios brain weight/body weight, indicated that

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[16] Snell, O., *Arch. Psychiatrie und Nervenkrankheiten*, **23**, 436 (1891).

[17] Du Bois, E., *Bull. Soc. Anthropol. Paris*, **8**, 337 (1897). Du Bois, E., "On the relation between the quantity of brain and the size of the body in vertebrates," *Proc. Koningl]ke Akad. Amsterdam*, **16**, 647 (1914), also **20**, 1328 (1918).

[18] Lapicque, L., *C. R., Soc. Biol.*, **50**, 62 (1898), and many papers since then. See especially Lapicque's chapter on the relation between brain weight and intelligence in "Traite de psychologie," Paris, 1922.

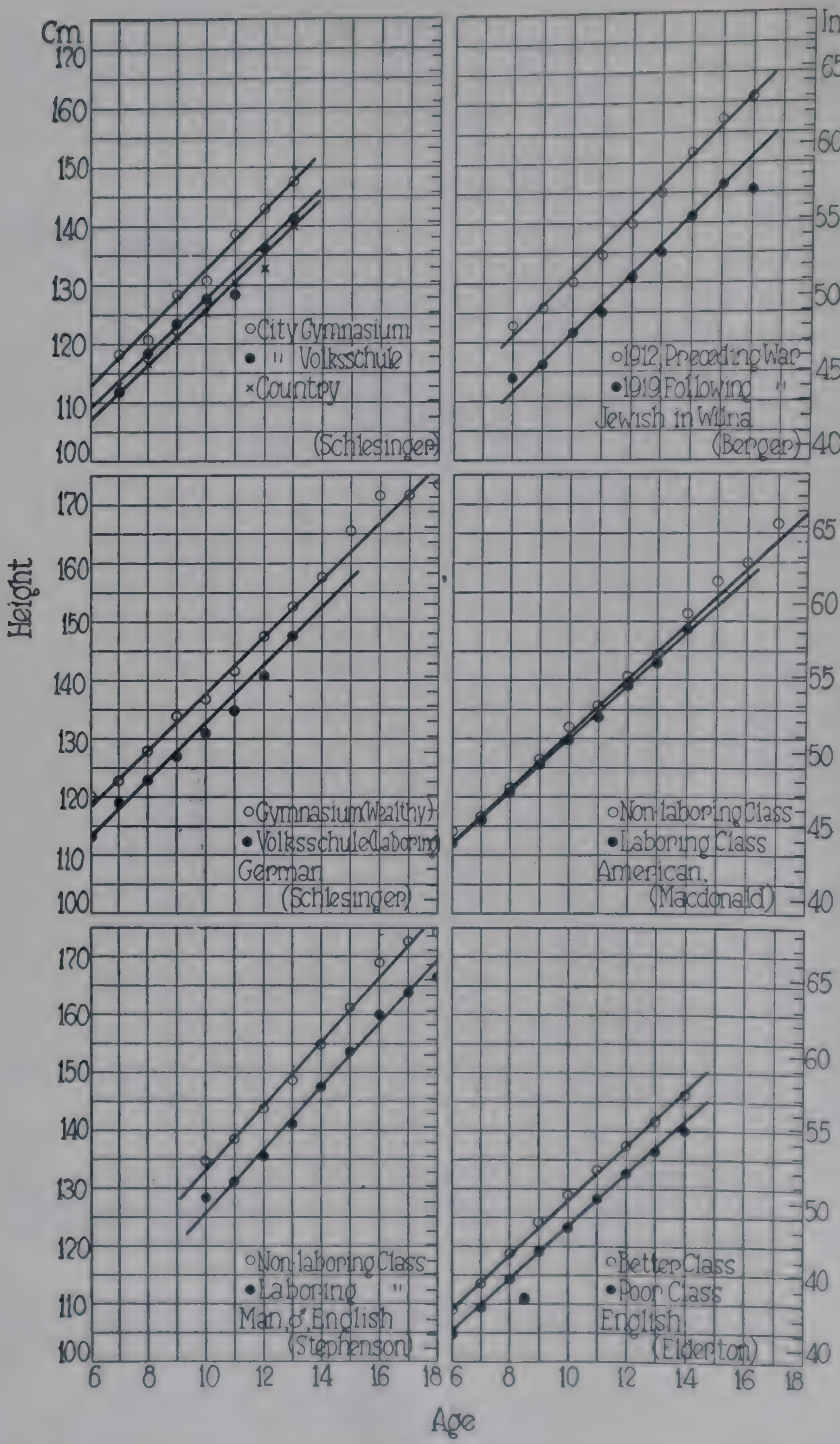

Fig. 17.14c. Juvenile growth in height of children is linear while weight growth is exponential (Fig. 16.50 and 16.52).

elephants had smaller brains and rats larger brains than man. Species comparisons of brain weights cannot be accomplished, therfore, by comparing absolute brain weights or by comparing the ratios of brain weight to simple body weight.

They next compared the power of brain weight to a power of body weight as indicated by the equation

$$Y_1 : Y_2 = X_1^b : X_2^b$$

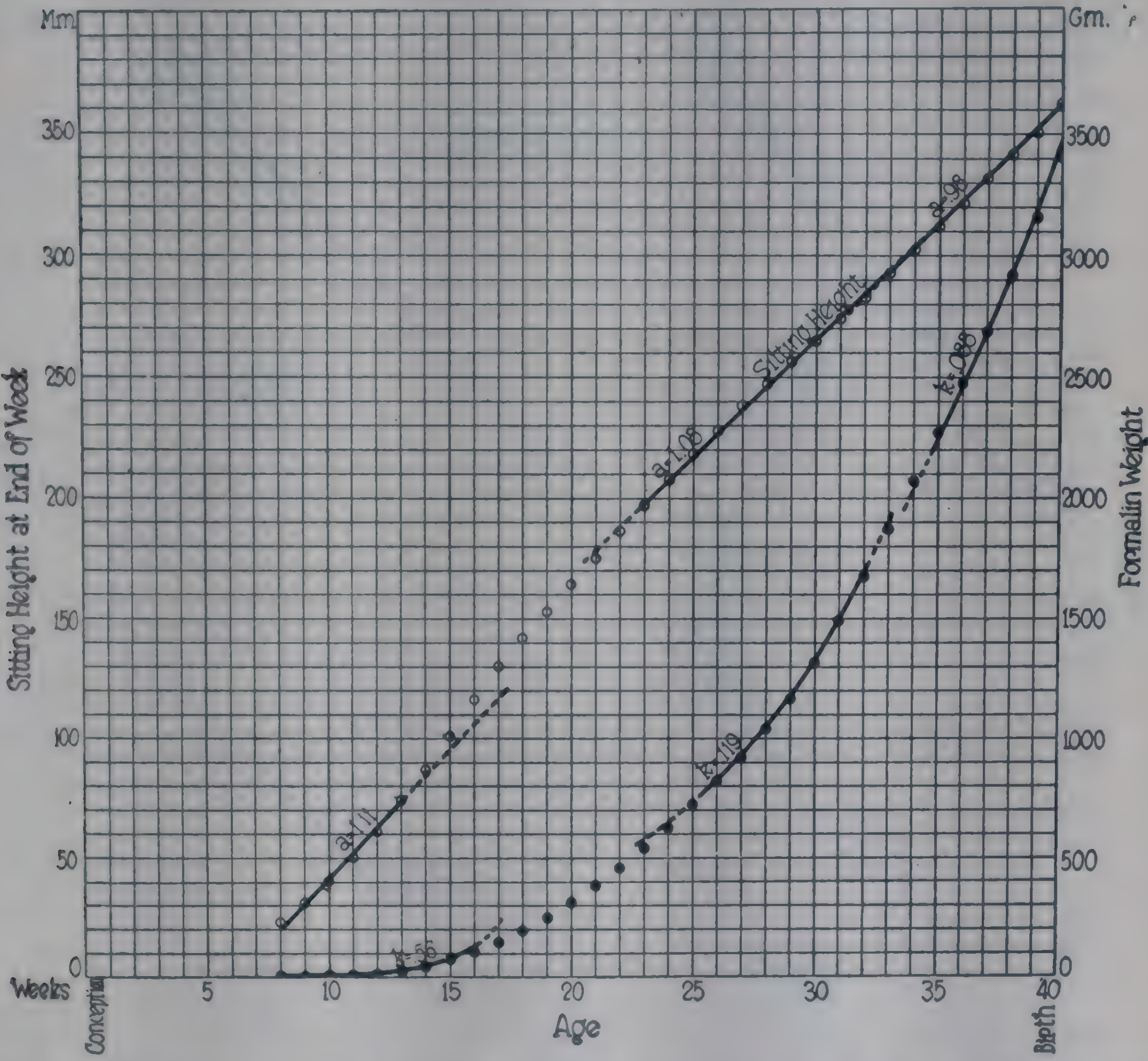

Fig. 17.14d. When prenatal weight growth (solid circles) in man is at a constant percentage rate, sitting-height growth (open circles) is linear. (From data by G. L. Streeter, Carnegie Inst. Washington, Contribution to *Embryology*, **11,** 143 (1920).

in which Y_1 and Y_2 are the brain weights of animals 1 and 2, having body weights X_1 and X_2.

The exponent b is evaluated by taking logarithms:

$$\log Y_1 - \log Y_2 = b \log X_1 - b \log X_2$$

whence

$$b = \frac{\log Y_1 - \log Y_2}{\log X_1 - \log X_2}$$

DuBois and Lapicque demonstrated in 1895 that the value of b was practically the same, of the order of 0.56, for many pairs of brain-body ratios of mature animals of *different species*, but only 0.25 for mature animals of the *same species*.

Lapicque, moreover, plotted the logarithms of brain weight against the logarithms of body weight and found that the distribution of the data is linear, having a slope of 0.56. He found that while the slope was always 0.56 for each of a number of series of animals, yet each of these closely related series of animals had a different intercept from other groups. That is, in the equation $Y = aX^b$, the numerical value of b was the same

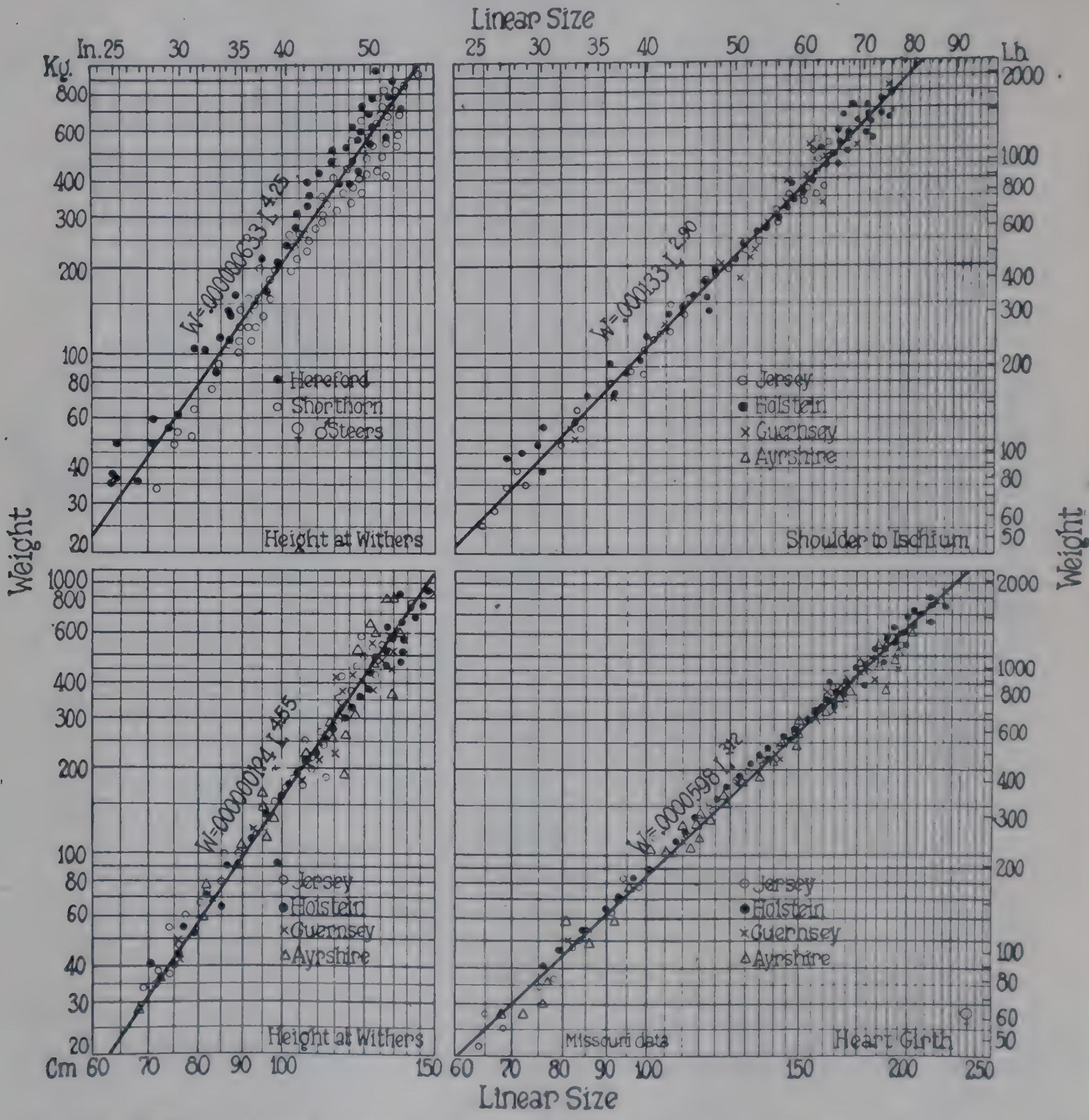

Fig. 17.15. The relation of weight to linear size in Jersey, Holstein, Guernsey, and Ayrshire cattle plotted on logarithmic coordinate paper.

for each of the series; but the numerical value of a, that is, the ratio $\frac{Y}{X^b} = a$, was highest for man; next for the anthropoid apes, and so on down the supposed scale of evolution.[19]

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[19] See Table 17.1, p. 642, and the charts for brain weights of different species. They show that a 60-kg man has about ten-fold the brain size of a 60 kg sheep—about 1500 gm, as contrasted to about 150 gm. Brain weight in man is about 1/40 of the body weight and 1/400 in other species of equal body weight. 1000-lb cattle have a brain weight of only 400 gm, horses 650 gm, and so on. Man's brain is almost as large as the elephant's (Fig. 10.1). In common words, a 150-lb man has a 3-lb brain; a 150-lb sheep has a ¼ lb brain; a 1500-lb cow has a one lb brain.

This discovery at once solved one of the great puzzles in anthropology, namely, why the ratio of brain size to simple body size of a fowl, for example, was as great as that of man.

Summarizing, Snell, DuBois, and Lapicque have shown that the proper method of comparing brain size to body size in animals of different size is not to evaluate the ratio of brain weight to simple body weight, but the ratio of brain weight to body weight raised to the *b*th power; and this ratio, a, the so-called "cephalization coefficient", in the equation $a = \frac{Y}{X^b}$, tends to vary with the degree of mental evolution. By this method the brain-to-body ratios met their expectation concerning differences in *relative* brain size in different species. The value of a in the ratio $\frac{Y}{X^b}$ is highest for man, a reassuring discovery.

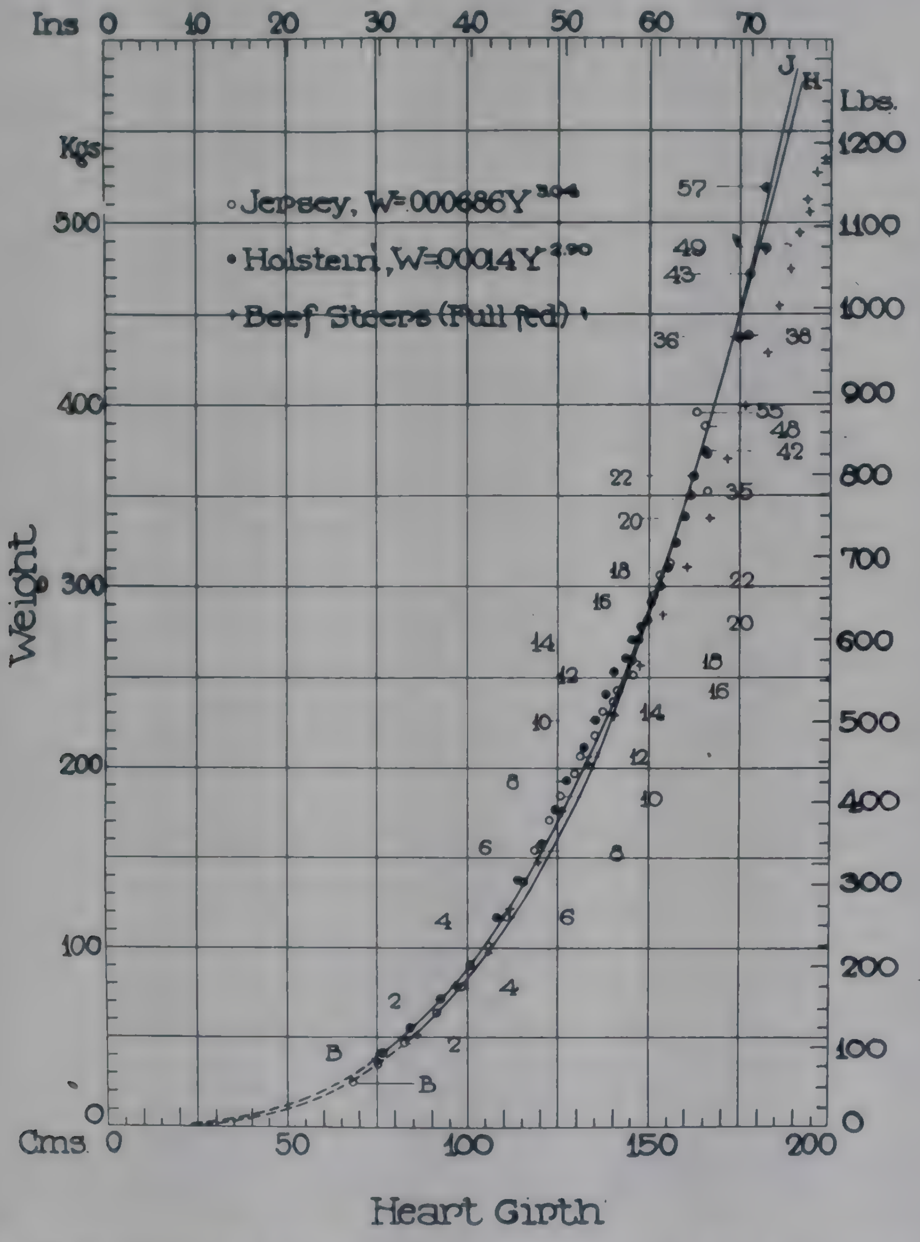

Fig. 17.16. The relation of weight to linear size in Jersey and Holstein cattle plotted on arithmetic coordinate paper. The numerals refer to the ages in months. Compare to Fig. 17.15 representing similar data on logarithmic paper.

This was, of course, the reasoning employed (Ch. 13) for comparing the metabolism of small and large animals. Thus the ratio metabolism Cal/body weight Kg is nearly

200 for mice and 15 for cattle; but the ratio metabolism Cal/(weight)^b Kg in which $b = 0.73$, is nearly the same, about 70, for both mice and cattle. It was, therefore concluded that the proper physiological reference base for comparing metabolism of mature animals of different species is not simple body weight, X, but the 0.73 power of body weight, that is $X^{0.73}$. As previously noted, dimensional consideration indicates an exponent of 0.67 for geometrically similar animals of different size; but large and small animals are not similar dimensionally.

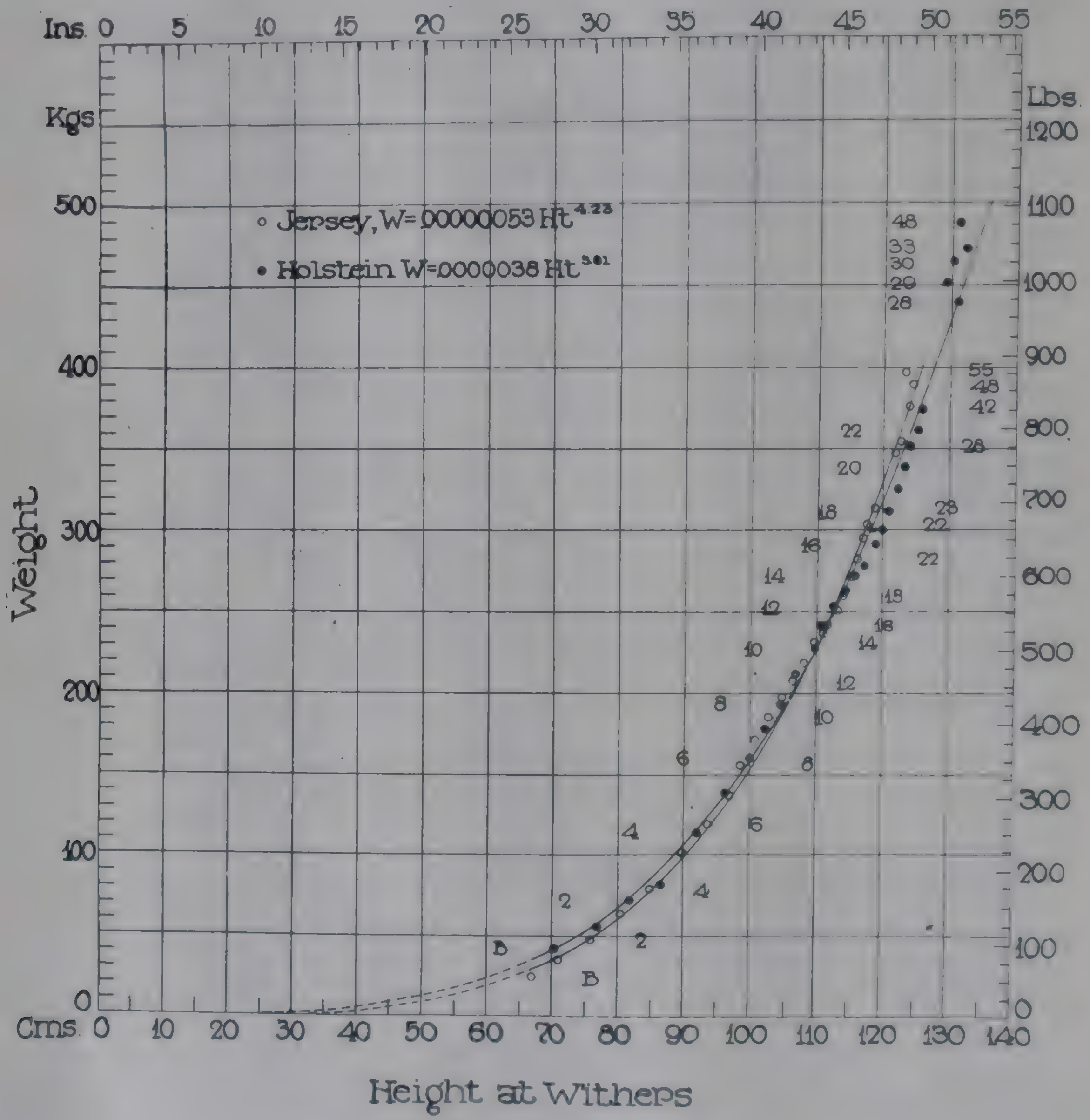

Fig. 17.17. See caption for Fig. 17.16.

The parabola $Y = aX^b$ has been used in biology for perhaps a century (Ch. 13) and since about 1890 for relating organ weight to body weight. About 1910 Dreyer[20] in England and Moulton and associates at the Missouri Station[21] became particularly active in its use. However, the impetus to its current popularity came from Huxley's[22] and Needham's[23] systematization, and nomenclature of data.

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[20] Dreyer, G., and Ray, W., *Proc. Roy. Soc.*, **82B**, 545 (1910), and many subsequent papers.

[21] Moulton, C. R., *J. Biol. Chem.*, **24**, 299 (1916). Trowbridge, P. F., Moulton, and Haigh, L. D., Univ. Mo. Agr. Exp. Sta. Res. Bull., 18, 1915. Brody, S., *et al.*, *Id.*, *Res. Bulls.*, 89, 1925; 115, 1928, 166, 1932 (pp. 89-97); 220, 1934; 262, 1937; 328, 1941.

As previously noted, the traditional name for the equation $Y = aX^b$ is parabola (b is positive), hyperbola (b is negative), linear (b is unity). However, name-minded biologists felt that a special terminology should be evolved, and many designations, for example allometry (Huxley and Teissier, 1936), from the Greek *allometron*, "that by which anything is measured", have been suggested. (The allometric equation $Y = aX^b$ is one "by which anything is measured"?) Since the writer's "competency" level does not react to these name "evocators", he will not discuss them, but proceed with analysis of relative-growth data with the aid of, as termed of old, parabolas, and refer the reader to the original papers for the newer terminology.[24]

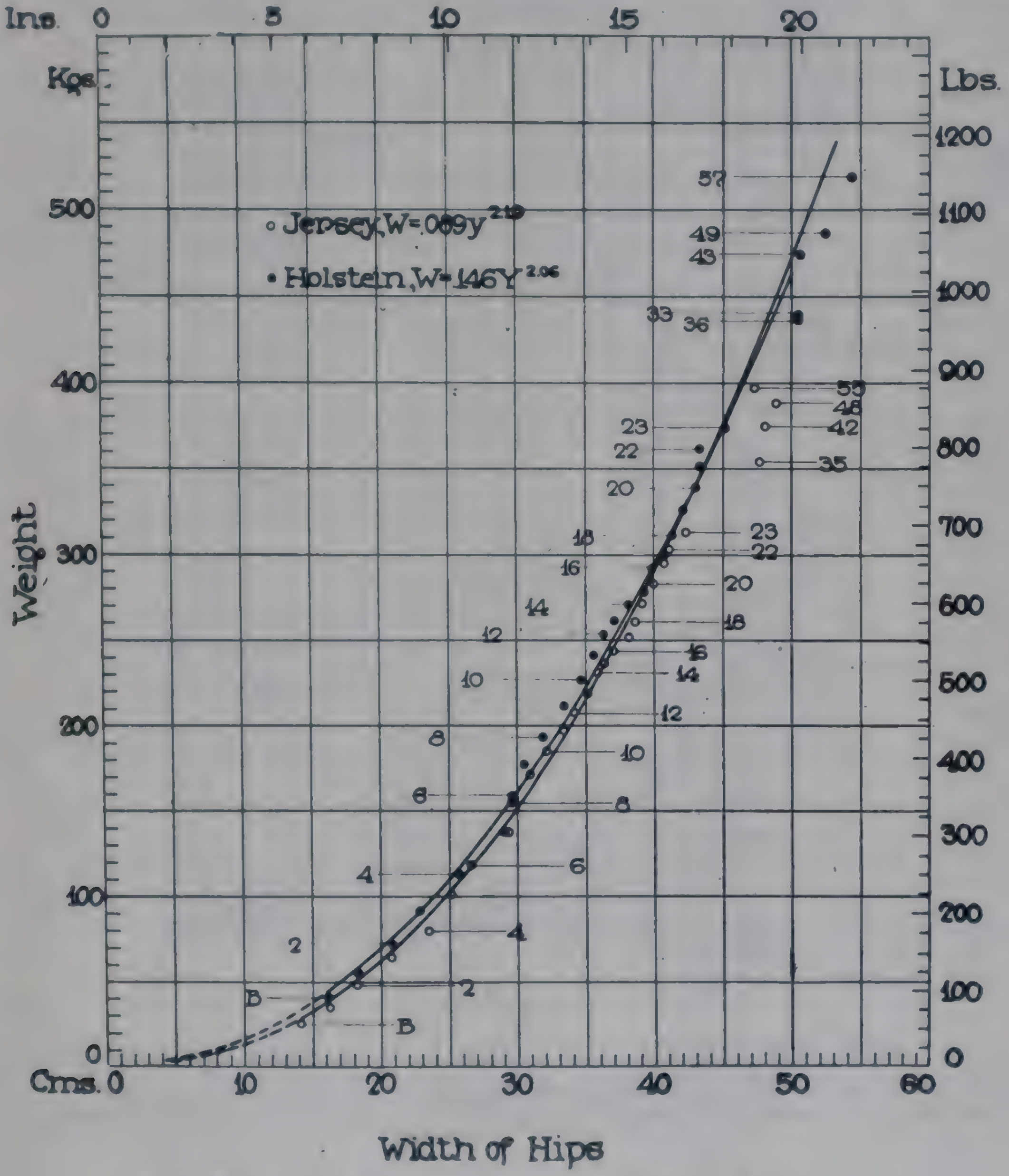

Fig. 17.18. See caption for Fig. 17.16.

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[22] Huxley, J. S., "Problems of relative growth," London, 1932.

[23] Needham, J., "Chemical Heterogony and the ground plan of animal growth," *Nature*, **130**, 845 (1932); *Biol. Rev.*, **9**, 79 (1934), and *Bull. Soc. Philomatique*, **11**, (1932).

[24] For the latest terminology of relative growth, see Needham, J., and Lerner, I. M., *Nature*, **146**, 618 (1940). For illustrative applications and references to literature, see Lerner, *Hilgardia*, **10**, no. 13 (1937). Hersh, A. H., *Growth*, **5**, (1941), supplement, p. 113. Richards, O., *Carnegie Inst. Washington, papers Tortugas Lab.*, **29**, 171 (1935), and (with A. J. Kavanagh) *Proc. Rochester (N. Y.) Acad Sci.*, **8**, 150 (1942).

17.4: Relation between organ weight and total body weight[25]. As explained above, the *relative* or *percentage growth* rates are different for linear size, area size, visceral organs, and total body weight. The extent of these differences in relative growth rate may be investigated by different methods.

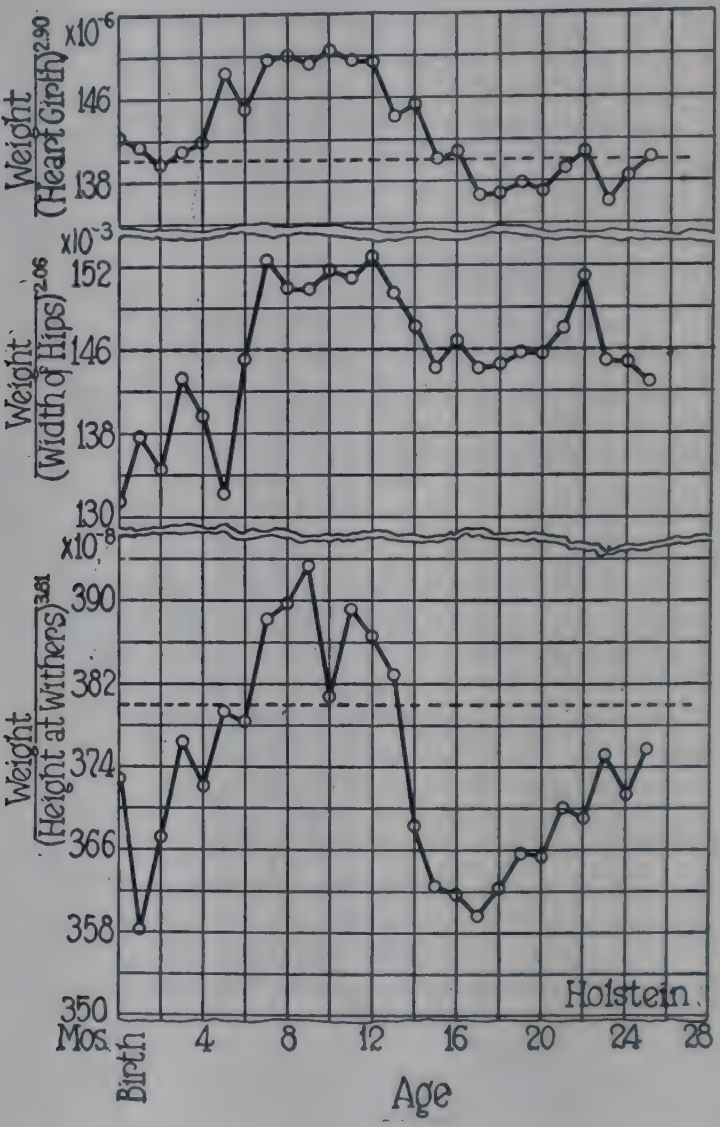

Fig. 17.19. While the curves in Figs. 17.15 to 17.18 appear entirely smooth, uneventful, yet if the ratios Y/X^b are plotted against age, trends appear. See, however, Fig. 17.25 representing a much greater body of different data, when trends disappeared.

One method (Figs. 17.1a and c), a qualitative one, consists in comparing outlines or photographs of the animal at different ages; a second method (Fig. 17.1b), semi-quantitative, consists in plotting the given measurements against age on arithlog paper (the slopes of which, of course, represent relative or logarithmic change) and comparing the slopes; or (Fig. 17.1d) plotting the given measurements in terms of percentages of mature size on arithmetic paper and comparing the slopes. The ratio of the slopes represents approximately the value of the exponent b in the equation $Y = aX^b$, as indicated below.

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[25] Brody, S., and Kibler, H. H., Univ. Mo. Agr. Exp. Sta. Res. Bull., 328, 1941.

A third method, illustrated in Figs. 17.2a and b, involves plotting against age the ratio of organ weight to body weight. This method appears simple, but it has disadvantages, one of which is that it is not possible to plot wide ranges of data on the same scale (Fig. 17.2b); another is that the eye is not as sensitive to deviations from a curve as it is from a straight line.

The fourth method, used exclusively in this chapter, attempts to "rectify" the data, that is throw them into a form which gives a straight line on some kind of paper. Thus the parabola $Y = aX^b$, and especially[26] $Y = aX^b + c$, is in straight-line form when written logarithmically: $\log Y = b \log X + \log a$. When plotted on log-log paper the data yield a straight-line distribution if the equation represents the data. However, there appear to be changes or "breaks" in the value of the exponent b, especially during early growth, as illustrated in Fig. 17.3. None the less, representation of the data on a log-log grid is the most satisfactory method; it shows how the

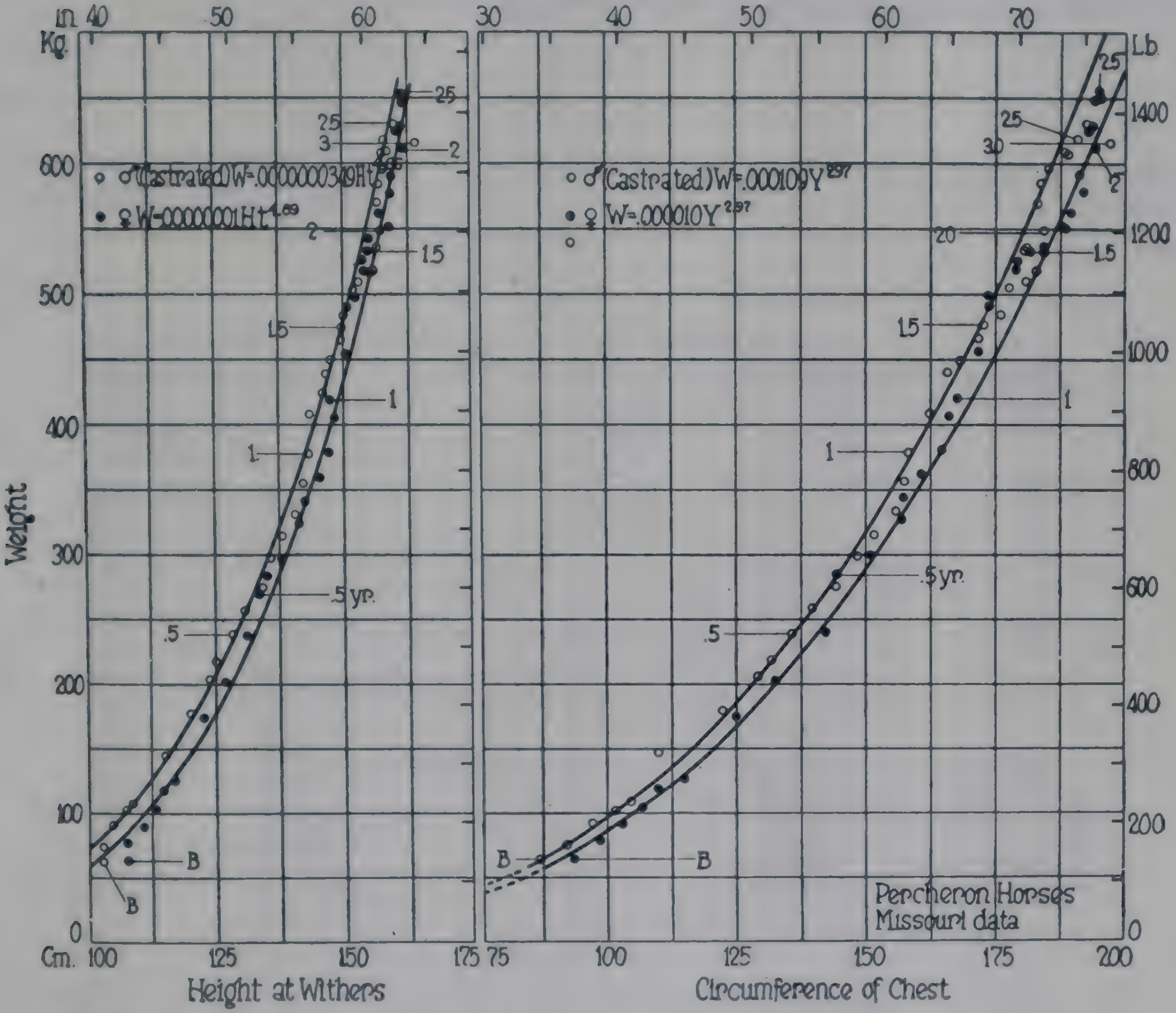

Fig. 17.20. The relations (slope) of weight to height at withers and to chest girth in work horses are almost identical with those in dairy cattle.

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[26] Robb, R. C., *British J. Exp. Biol.*, **6**, 311 (1929). Twitty, C., *Symposia on Quant. Biol.*, **2**, 148 (1934).

percentage increase in organ weight changes with percentage increase in body weight. The values of the slopes, b, given in Fig. 17.3, were computed by the usual method, $b = \dfrac{\log Y_1 - \log Y_2}{\log X_1 - \log X_2}$.

Derivation of the parabola Y = aX^b from the exponential growth equation. Preceding the inflection in the S-shaped age curve of growth in weight (self-accelerated phase), the course of growth may be represented by the equations:

$$Y = c_1 e^{k_1 t} \tag{1}$$

$$X = c_2 e^{k_2 t} \tag{2}$$

where Y is the size of one structure; X, the size of another structure; c_1 and c_2 constants; k_1 and k_2, growth rates; t, time or age. Taking natural logarithms of (1) and (2),

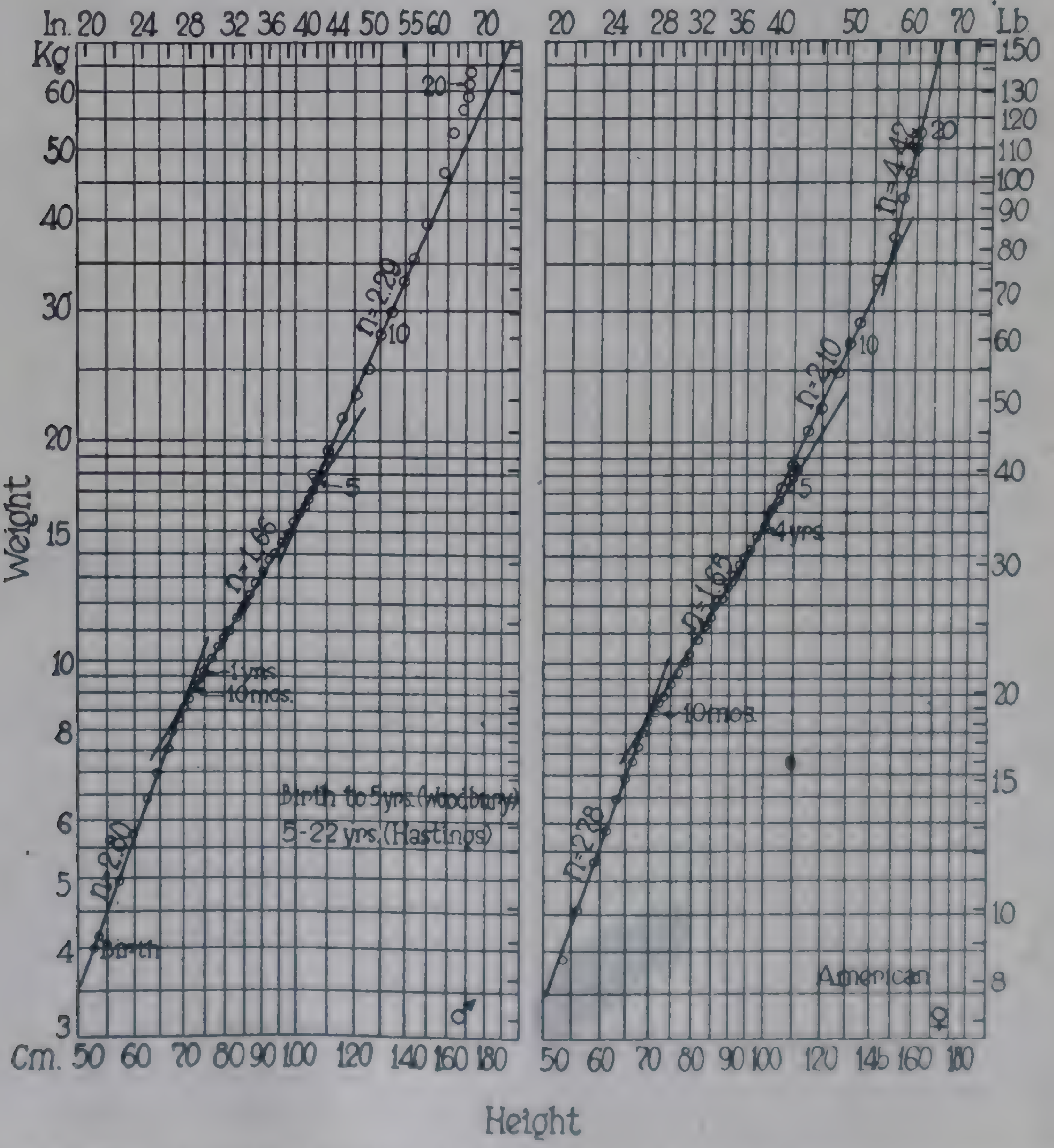


Fig. 17.21. The relation of weight to height in man plotted on logarithmic coordinate paper. The curve appears to have four segments, each having a different slope, n.

$$\ln Y = \ln c_1 + k_1 t$$

$$\ln X = \ln c_2 + k_2 t$$

Differentiating

$$\frac{dy}{y} = k_1\,dt \tag{3}$$

$$\frac{dx}{x} = k_2\,dt \tag{4}$$

Dividing (3) by (4)

$$\frac{dy}{y} \div \frac{dx}{x} = \frac{k_1}{k_2} \qquad \text{or} \qquad \frac{dy}{y} = b\,\frac{dx}{x}$$

where $\frac{k_1}{k_2} = b$ (a constant).

Integrating

$$\log Y = b \log X + \log a$$

and

$$Y = aX^b$$

which is our parabola.

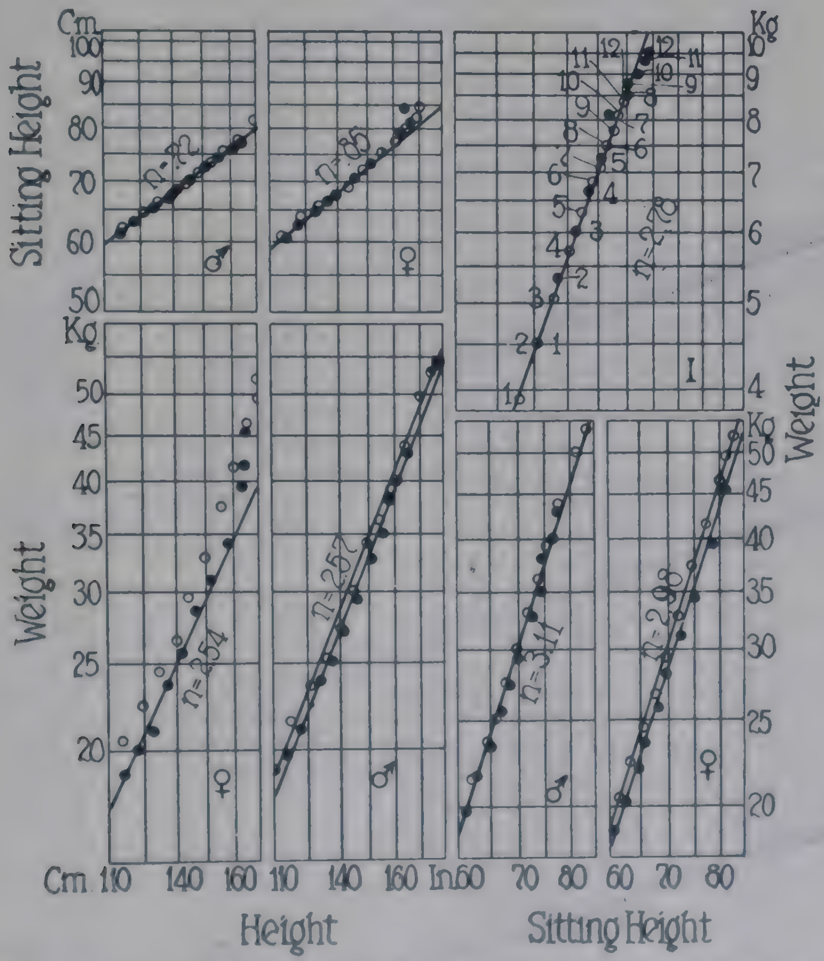
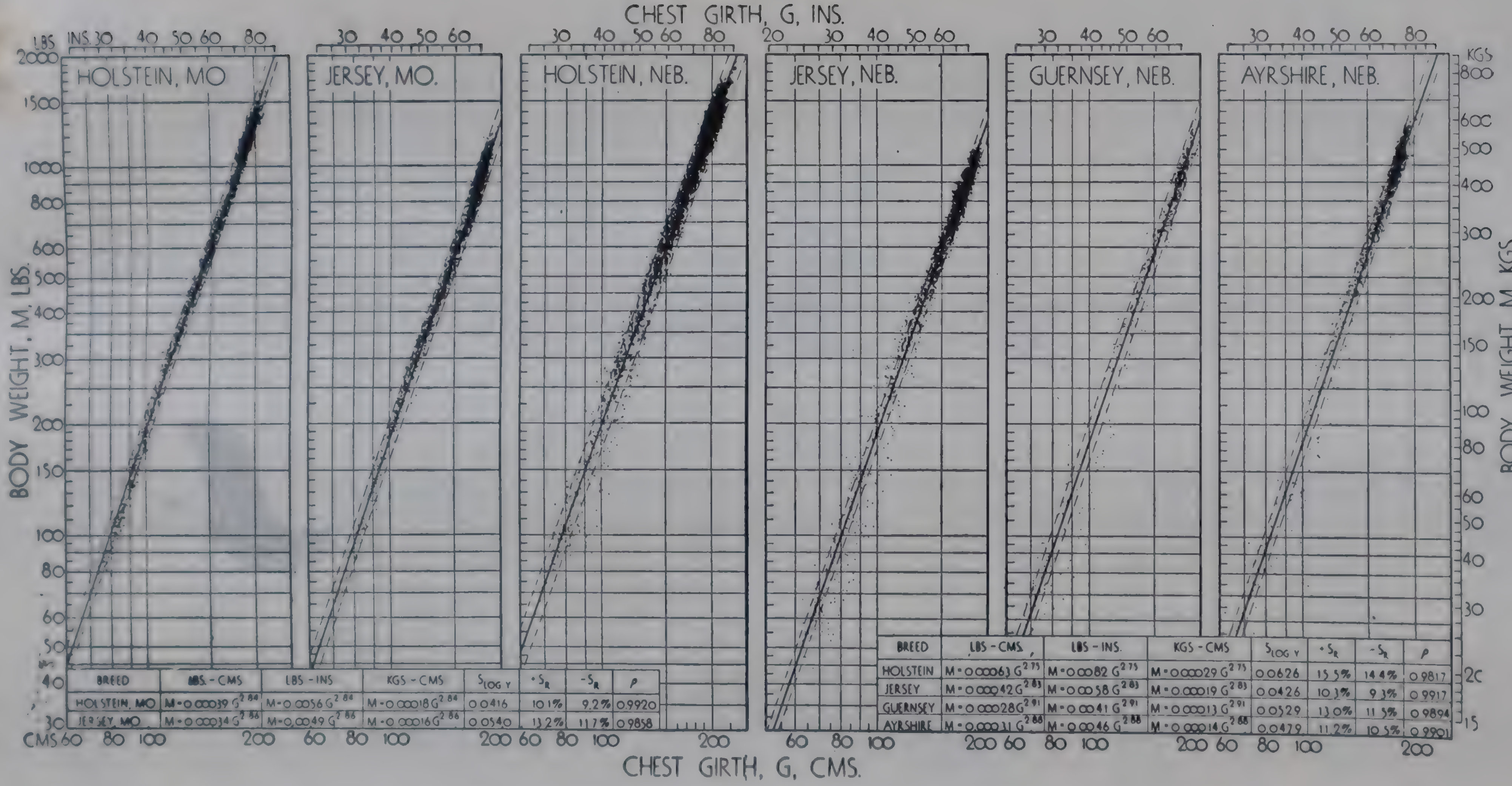


Fig. 17.22. The relation of weight to height and to sitting height; also of sitting height to height, for children in different economic classes, plotted on logarithmic coordinate paper. The slopes, n, are indicated on each curve.



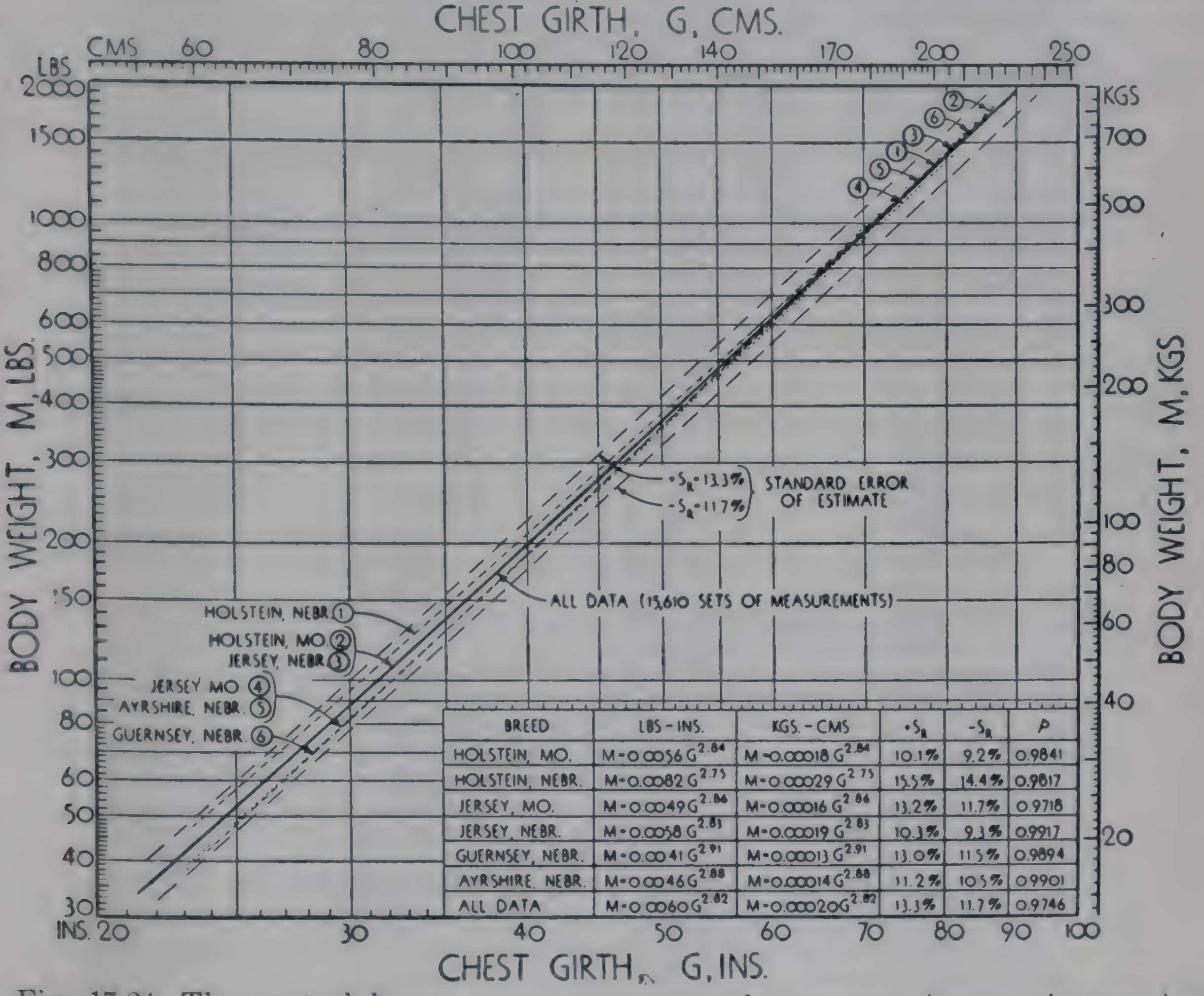
BREED	LBS. - CMS	LBS - INS	KGS - CMS	$S_{\log Y}$	$+S_R$	$-S_R$	ρ
HOLSTEIN, MO	$M = 0.00039\,G^{2.84}$	$M = 0.0056\,G^{2.84}$	$M = 0.00018\,G^{2.84}$	0.0416	10.1%	9.2%	0.9920
JERSEY, MO	$M = 0.00034\,G^{2.86}$	$M = 0.0049\,G^{2.86}$	$M = 0.00016\,G^{2.86}$	0.0540	13.2%	11.7%	0.9858

BREED	LBS - CMS	LBS - INS.	KGS - CMS	$S_{\log Y}$	$+S_R$	$-S_R$	ρ
HOLSTEIN	$M = 0.00063\,G^{2.75}$	$M = 0.0082\,G^{2.75}$	$M = 0.00029\,G^{2.75}$	0.0626	15.5%	14.4%	0.9817
JERSEY	$M = 0.00042\,G^{2.83}$	$M = 0.0058\,G^{2.83}$	$M = 0.00019\,G^{2.83}$	0.0426	10.3%	9.3%	0.9917
GUERNSEY	$M = 0.00028\,G^{2.91}$	$M = 0.0041\,G^{2.91}$	$M = 0.00013\,G^{2.91}$	0.0529	13.0%	11.5%	0.9894
AYRSHIRE	$M = 0.00031\,G^{2.88}$	$M = 0.0046\,G^{2.88}$	$M = 0.00014\,G^{2.88}$	0.0479	11.2%	10.5%	0.9901

Fig. 17.23. The relation of body weight to chest girth in dairy cattle. This chart includes 15,610 data points. The heavy line represents the parabola $Y = aX^b$ fitted to the data by the method of least squares. The light broken lines represent the standard error of estimate, S_R, including ⅔ of the data point. The constant rho, ρ, corresponds to the coefficient of correlation, r, for linear equations.

It is more confusing to derive the parabola from the equation for the phase of growth following the inflection[26a] (self-inhibited growth phase).

The inflection in the S-shaped curve of growth in total weight does not necessarily coincide with the inflections in growth of the bodily components or with the age curves of the several linear dimensions. Moreover, the course of weight growth prior to the inflection tends to be exponential, while that of linear growth tends to be linear (see section below on linear growth). It follows that while the parabola $Y = aX^b$ may fit the relation approximately, or for segments of the curve, it cannot represent precisely the $Y - X$ relation for the entire growth period. There must be "breaks" or changes in slope in the curve, perhaps insignificant, as was indeed demonstrated by Lumer.[27] This parabola is none the less extremely useful.



BREED	LBS - INS.	KGS. - CMS	$+S_R$	$-S_R$	ρ
HOLSTEIN, MO.	$M = 0.0056\,G^{2.84}$	$M = 0.00018\,G^{2.84}$	10.1%	9.2%	0.9841
HOLSTEIN, NEBR.	$M = 0.0082\,G^{2.75}$	$M = 0.00029\,G^{2.75}$	15.5%	14.4%	0.9817
JERSEY, MO.	$M = 0.0049\,G^{2.86}$	$M = 0.00016\,G^{2.86}$	13.2%	11.7%	0.9718
JERSEY, NEBR.	$M = 0.0058\,G^{2.83}$	$M = 0.00019\,G^{2.83}$	10.3%	9.3%	0.9917
GUERNSEY, NEBR.	$M = 0.0041\,G^{2.91}$	$M = 0.00013\,G^{2.91}$	13.0%	11.5%	0.9894
AYRSHIRE, NEBR.	$M = 0.0046\,G^{2.88}$	$M = 0.00014\,G^{2.88}$	11.2%	10.5%	0.9901
ALL DATA	$M = 0.0060\,G^{2.82}$	$M = 0.00020\,G^{2.82}$	13.3%	11.7%	0.9746

Fig. 17.24. The central heavy curve represents the average (geometric mean) of all the 15,610 data points. The lighter lines represent the curves from Fig. 17.23, and the standard error of estimate.

Let us next picture the situation as a whole: how a set of organs in a given species grows in relation to the body as a whole. Such a general picture is shown in Fig. 17.4 for the growth of man, birth to 20 years of age. From this chart, it will be seen that the brain grows about 70 per cent as rapidly as the body prior to about 6 years and about 7 per cent as rapidly thereafter. The slope declines from about 70 to about 7 per cent, an enormous "break".

[26a] For its derivation, see Univ. Mo. Agr. Exp. Sta. Res. Bull., 262, 1937.

[27] Bernstein, F., *Symposia on Quantitative Biology*, **2**, 209 (1934); Lumer, H., *Growth*, **1**, 140 (1937). Brody, S., Davis, H. P., and Ragsdale, A. C., Univ. Mo. Agr. Exp. Sta. Res. Bull., 262, 1937.

The curve for the liver also appears to show a break at about 6 years.

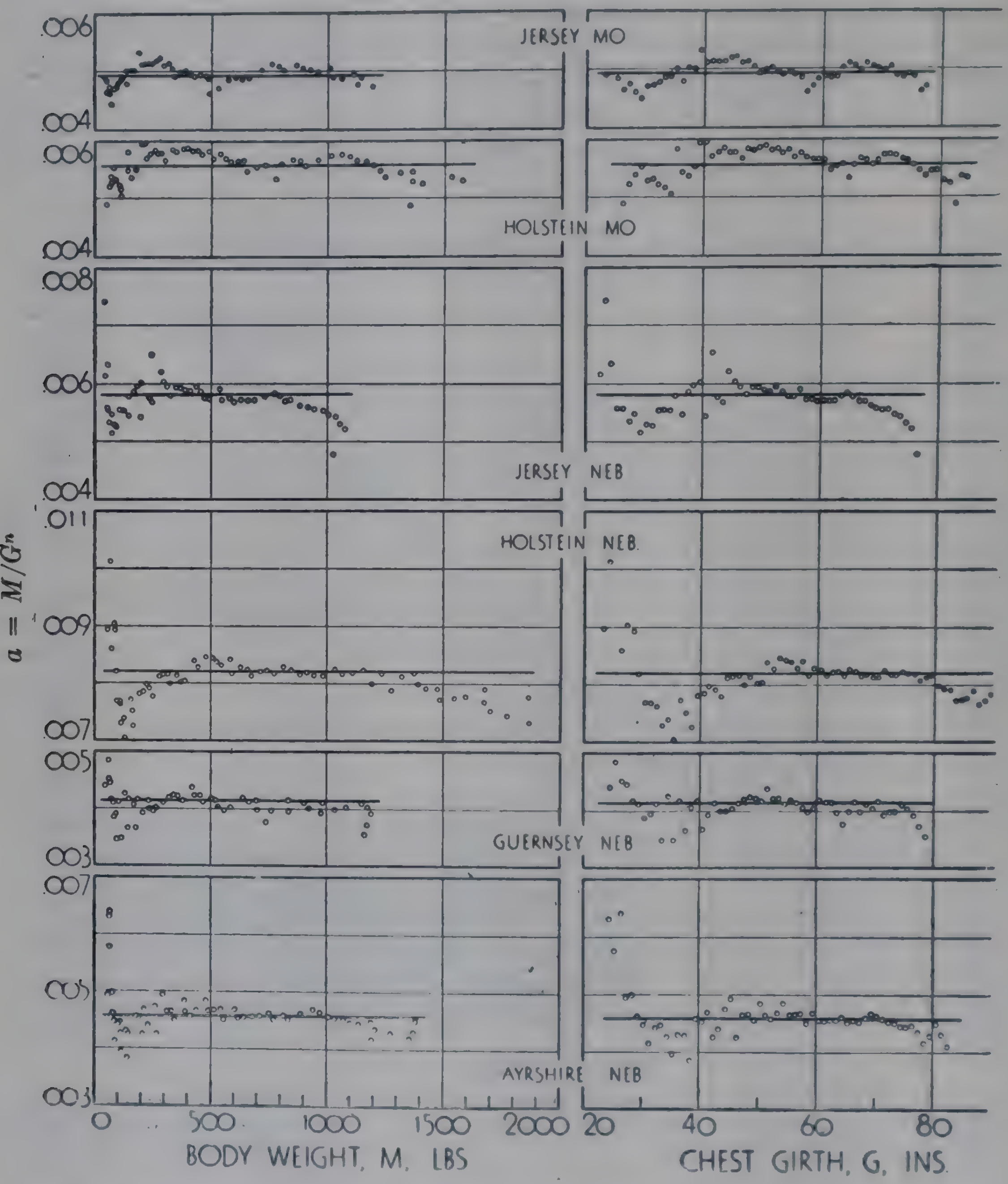
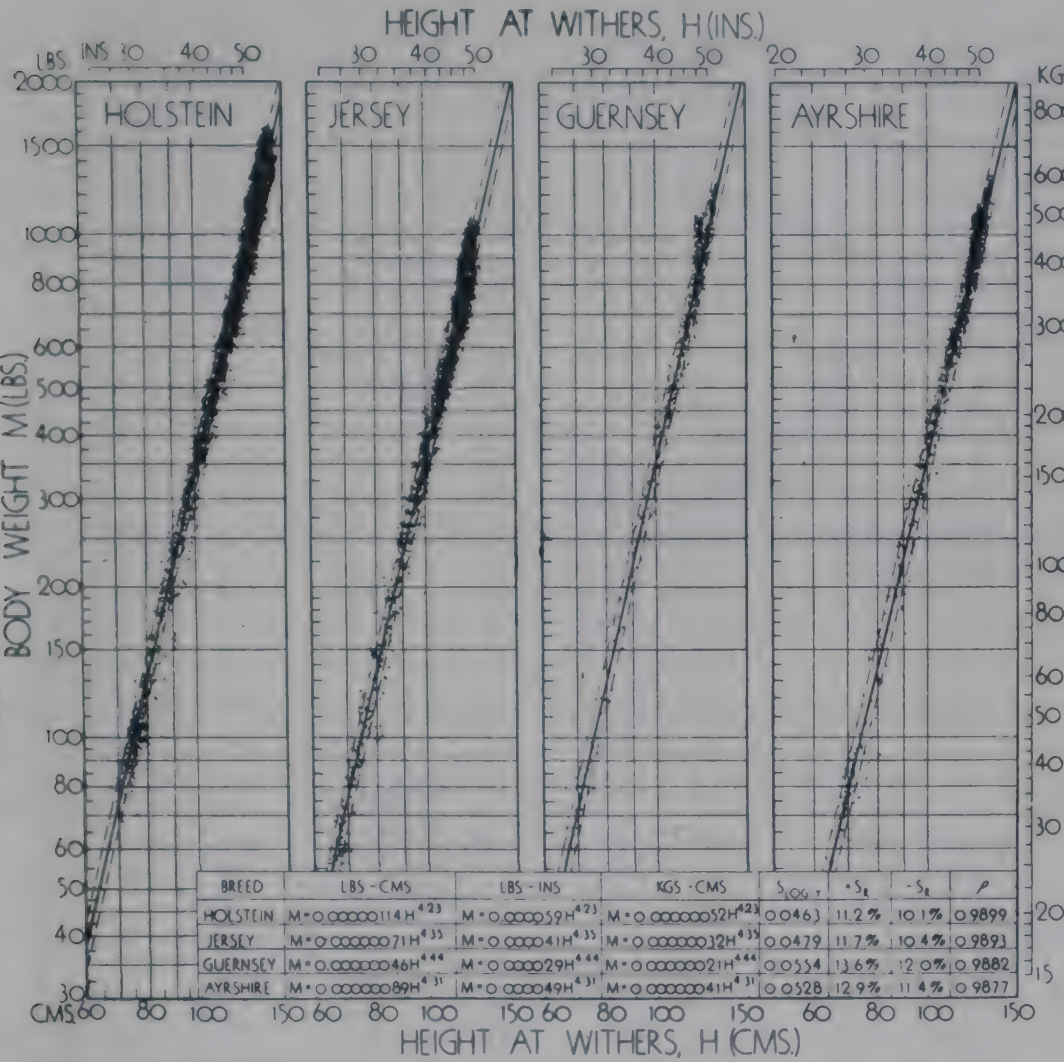


Fig. 17.25. The nature of the fluctuations in the ratio $\frac{\text{weight}}{(\text{chest girth})^b}$ for the data in Fig. 17.23 indicates that either there are no biologically-significant systematic deviations from the parabolic trend $Y = aX^b$, or that the fluctuations are masked by compensation. See, however, Fig. 17.19 representing a different set of data.

With the exception of heart, thyroid, and spleen, the relative increase in the weight of the visceral organs is less than that of the body as a whole.

The gonads and adrenals follow a parallel course: they rise, first slowly then rapidly, on to the advent of puberty. It did not seem worthwhile to fit equations to the data. The gonads in rabbits[27a] increase during a certain age interval, with the X^2 for females and $X^{2.8}$ for males; the adrenals in the same rabbits increased with $X^{0.9}$ for both males and females (X = body weight). A curious feature of the rabbit adrenal curve is that at about 2.5 kg body weight (beginning of sex activity), there is an increase in slope of the adrenal curve; the adrenal weight then increases with $X^{1.78}$ instead of with $X^{0.94}$ (Fig. 17.5b). The same results were obtained on guinea pigs (Fig. 17.5d).[28] This sudden increase in adrenal weight may be associated with a corresponding acceleration in protein catabolism[29], and hence with a decline in growth rate at this time. Some animals also show a steep rise in the kidney weight at this time (Fig. 17.5e).

[27a] Kibler, H. H., Bergman, A. J., and Turner, C. W., *Endocrinology*, **33**, 250 (1943).



BREED	LBS - CMS	LBS - INS	KGS - CMS	$S_{\log Y}$	$+S_R$	$-S_R$	ρ
HOLSTEIN	$M = 0.00000114H^{4.23}$	$M = 0.000059H^{4.23}$	$M = 0.00000052H^{4.23}$	0.0463	11.2%	10.1%	0.9899
JERSEY	$M = 0.00000071H^{4.35}$	$M = 0.000041H^{4.35}$	$M = 0.00000032H^{4.35}$	0.0479	11.7%	10.4%	0.9893
GUERNSEY	$M = 0.00000046H^{4.44}$	$M = 0.000029H^{4.44}$	$M = 0.00000021H^{4.44}$	0.0554	13.6%	12.0%	0.9882
AYRSHIRE	$M = 0.00000089H^{4.31}$	$M = 0.000049H^{4.31}$	$M = 0.00000041H^{4.31}$	0.0528	12.9%	11.4%	0.9877

Fig. 17.26. The relation of body weight to height at withers. Note that the fit of the parabola $Y = aX^b$ is not as good for the weight to height as for the weight to chest girth.

Fig. 17.4 thus indicates the general course and the order of change of organ weight with increase in body weight during growth, the nature of the breaks in the curve, the nature of changes in "atypical" curves, such as of the gonads and adrenals, and incidentally gives an idea of the weights of the various organs.

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[28] Mixner, J. P., Bergman, A. J., and Turner, C. W., *Endocrinology*, **32**, 298 (1943).

[29] *Cf.* Long, C. N. H., "Cortical hormones and metabolism," *Endocrinology*, **30**, 870 (1942). Turner, C. W., Personal communication.

As explained above, the value of the exponent, b, in the equation $Y = aX^b$, varies with age and with other factors. Fig. 17.6 shows the values of b for various organs in dairy cattle, in this case all mature, and ranging in body weight (at the slaughter house) from 800 to 1600 lbs. Here the slope b is very low for all organs. Thus the heart varies with $X^{0.56}$ rather than with $X^{1.02}$, as in growing man (see Table 17.1).

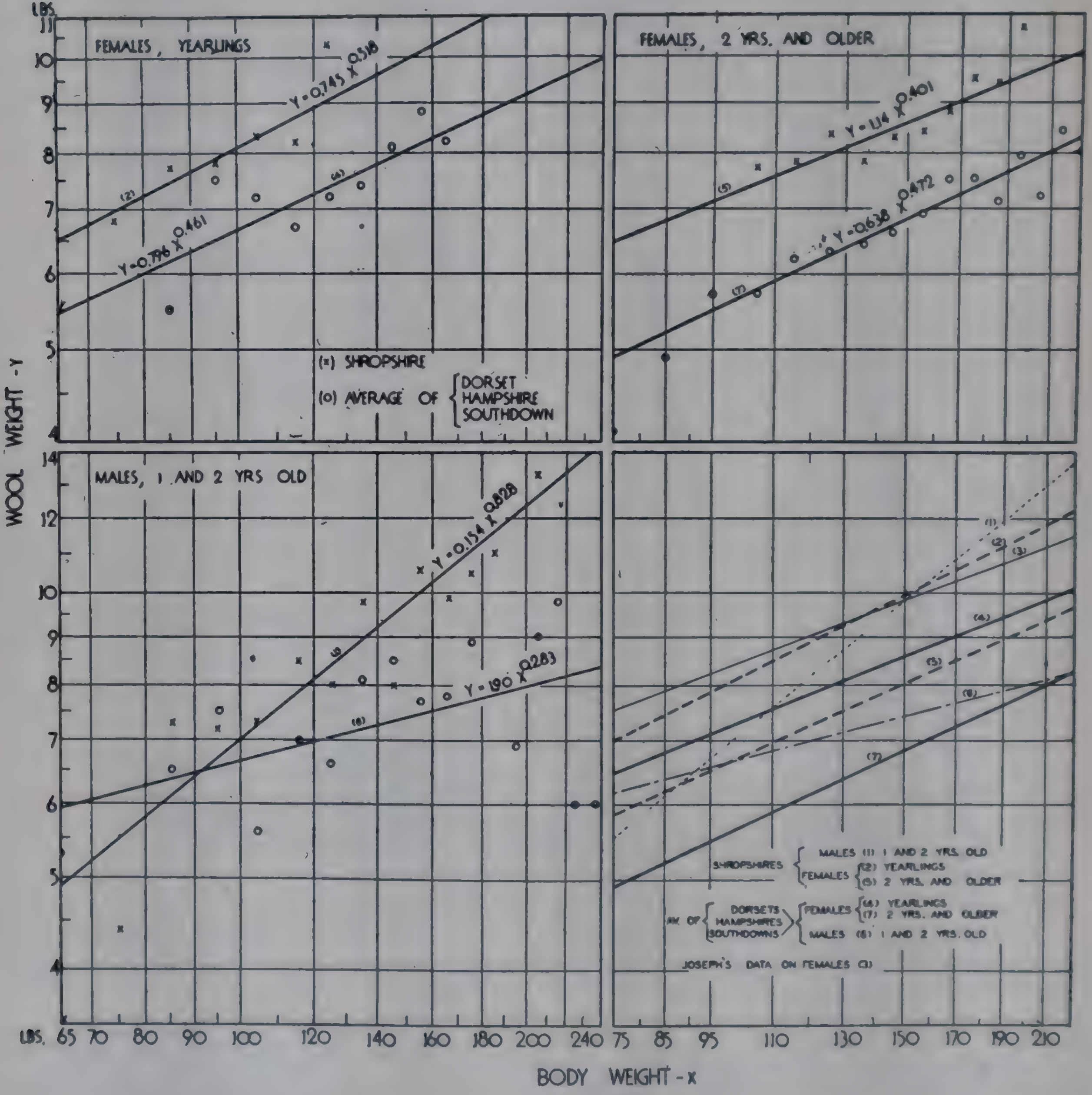
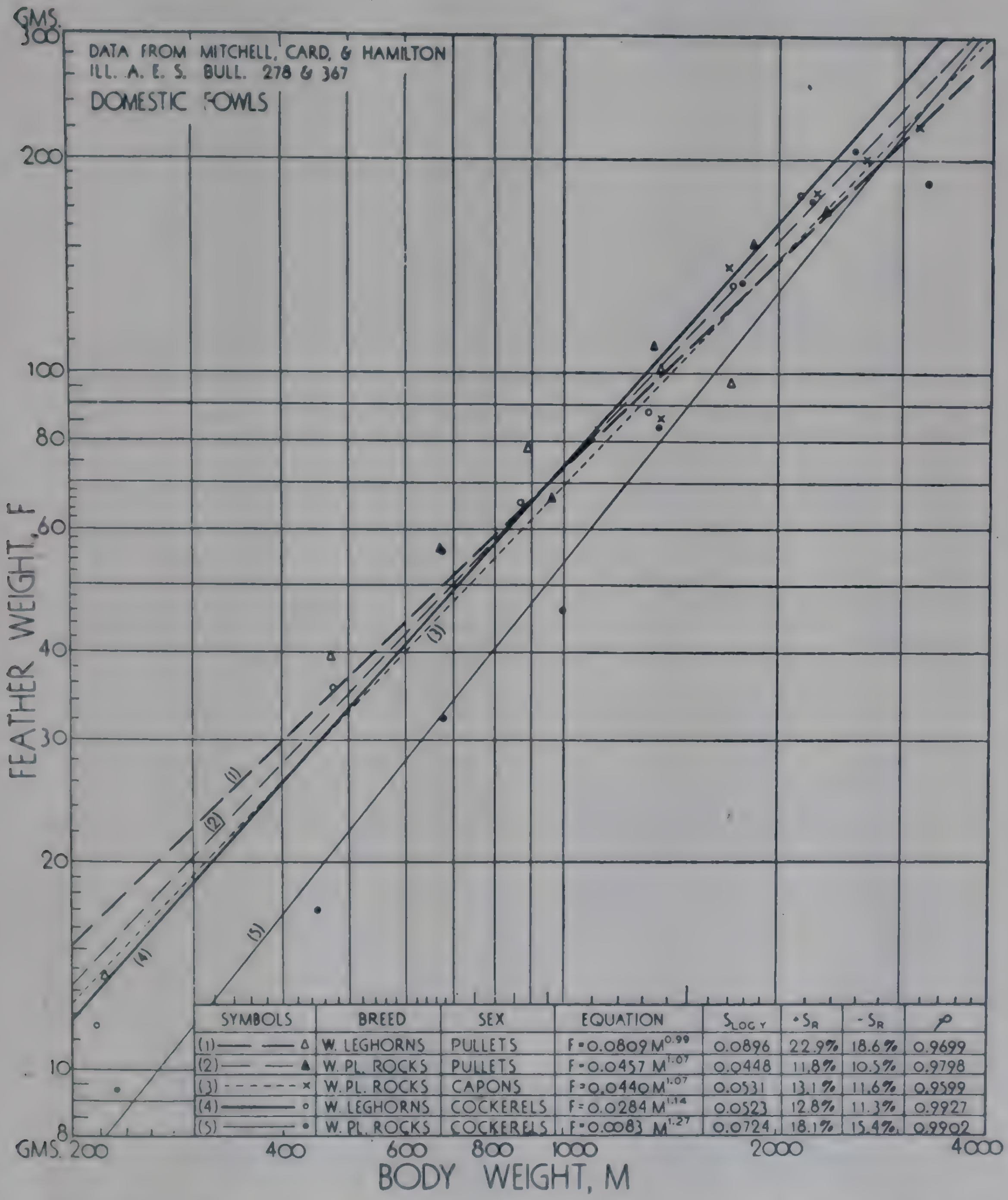


Fig. 17.27. Wool weight as function of body weight.

So far we discussed the relation of organ weight to body weight in the same species. Fig. 17.7 shows the relation of organ weight to body weight in mature mammals (heavy lines) and birds (light broken lines) of different species. The slopes, b, are given on the chart (see Table 17.4).

Fig. 17.7 shows that for mature mammals of different species, the basal heat production increases with the 0.73 power of body weight; the brain weight increases with the 0.70 power of body weight, virtually the same as for basal heat production; the pituitary increases with the 0.76 power of body weight; the adrenals with the 0.80 power, and so on. Without exception the visceral organ weights in *mature animals* of *different species*[30] increase with a fractional power of body weight, that is, the weights of visceral organs do not increase as rapidly as the body as a whole.



SYMBOLS	BREED	SEX	EQUATION	$S_{LOG\ Y}$	$+S_R$	$-S_R$	ρ
(1) — — △	W. LEGHORNS	PULLETS	$F = 0.0809 M^{0.99}$	0.0896	22.9%	18.6%	0.9699
(2) — — ▲	W. PL. ROCKS	PULLETS	$F = 0.0457 M^{1.07}$	0.0448	11.8%	10.5%	0.9798
(3) - - - - - - ×	W. PL. ROCKS	CAPONS	$F = 0.0440 M^{1.07}$	0.0531	13.1%	11.6%	0.9599
(4) —— ○	W. LEGHORNS	COCKERELS	$F = 0.0284 M^{1.14}$	0.0523	12.8%	11.3%	0.9927
(5) —— ●	W. PL. ROCKS	COCKERELS	$F = 0.0083 M^{1.27}$	0.0724	18.1%	15.4%	0.9902

Fig. 17.28a. Feather weight, F, in chickens plotted against body weight, M.

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[30] The most important, indeed monumental, collection of data on organ size is given by Crile, George, and Quiring, D. P., *Ohio J. Soc.*, **40**, 219 (1940).

The most conspicuous feature is that the slope of the curve relating brain weight to body weight is virtually the same as the slope relating basal heat production to body weight. This means that the ratio metabolic rate/brain

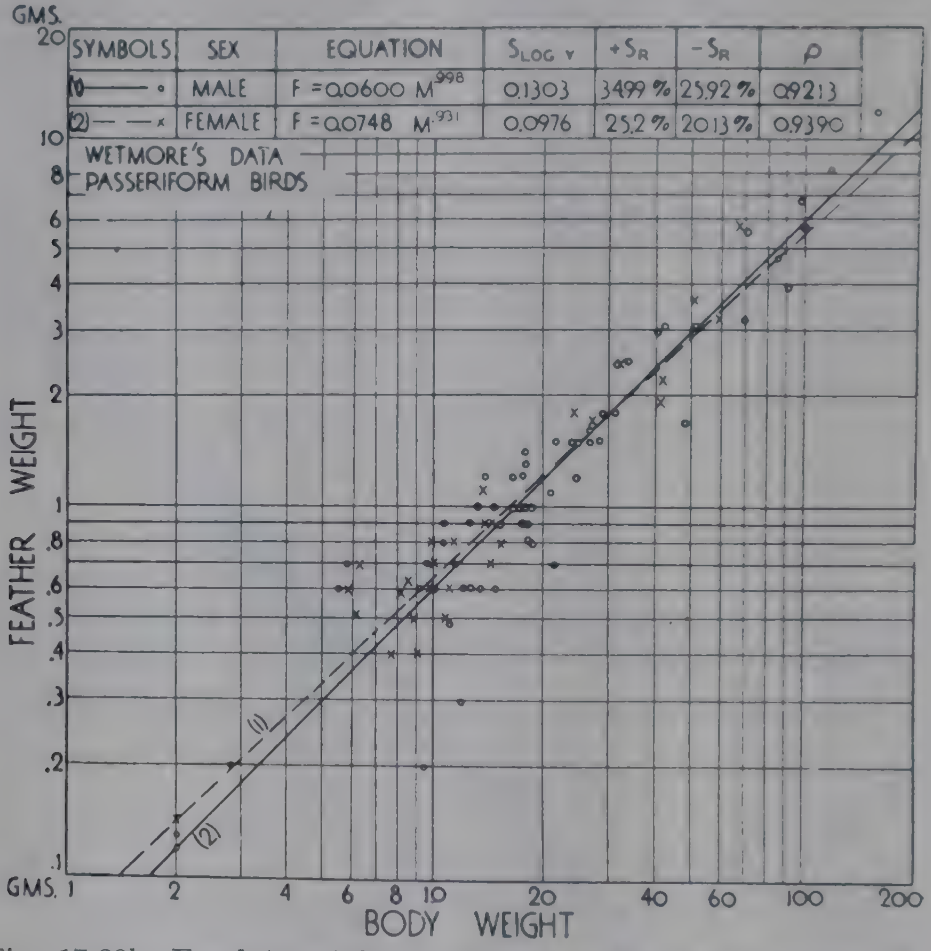

Fig. 17.28b. Feather weight, F, plotted against body weight, M.

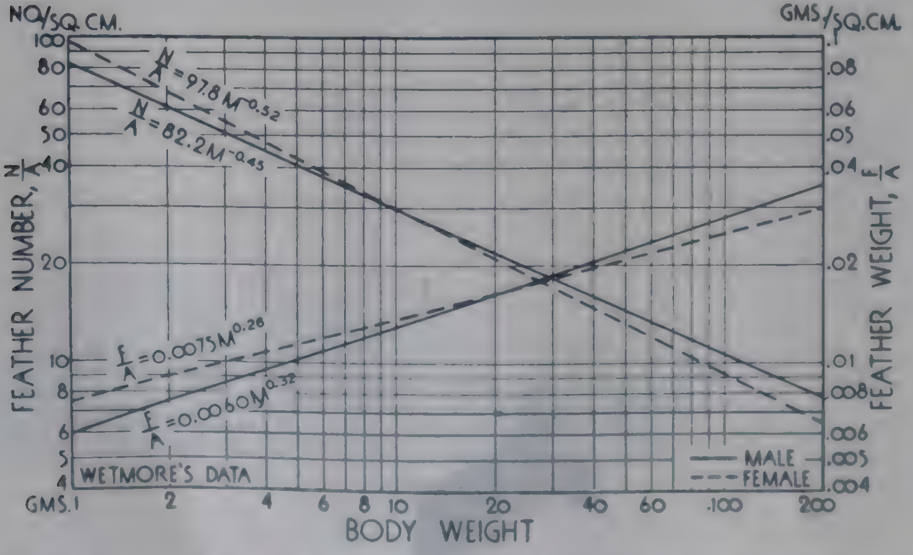

Fig. 17.28c. Feather number and feather weight per unit surface area, plotted against body weight.

weight tends to be the same for small and large animals; the ratio metabolic rate/body weight, on the other hand, declines rapidly with increasing weight.

Does this close *statistical* correlation imply the presence of a similarly close *causal physiological* interrelation between brain weight and metabolism?

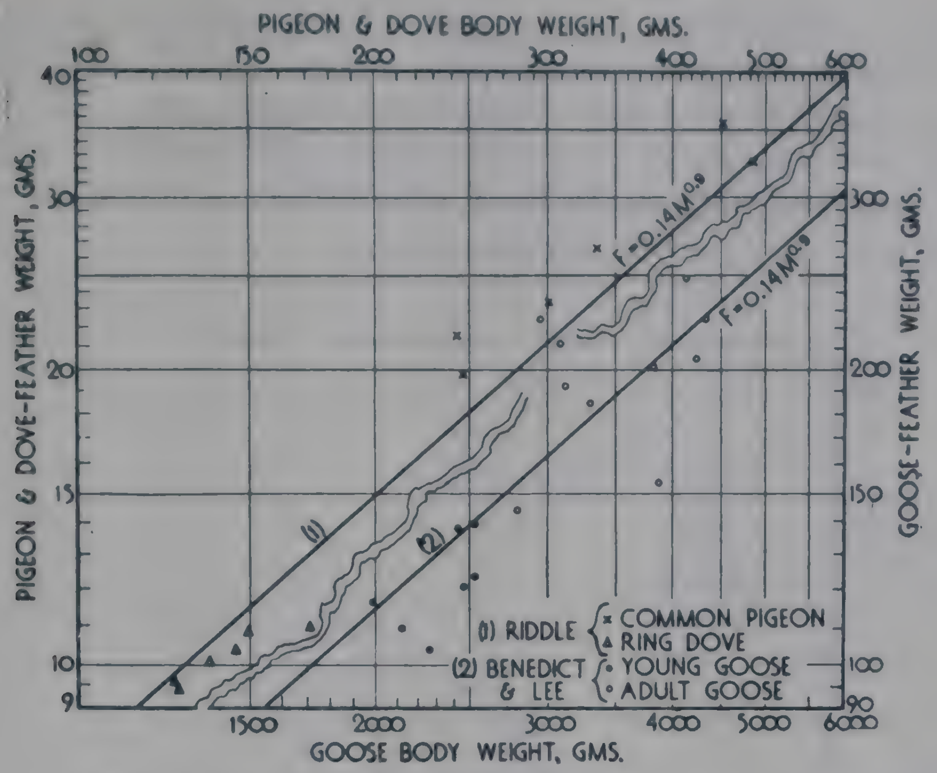

Fig. 17.28d. See caption for Figs. 17.28a and b.

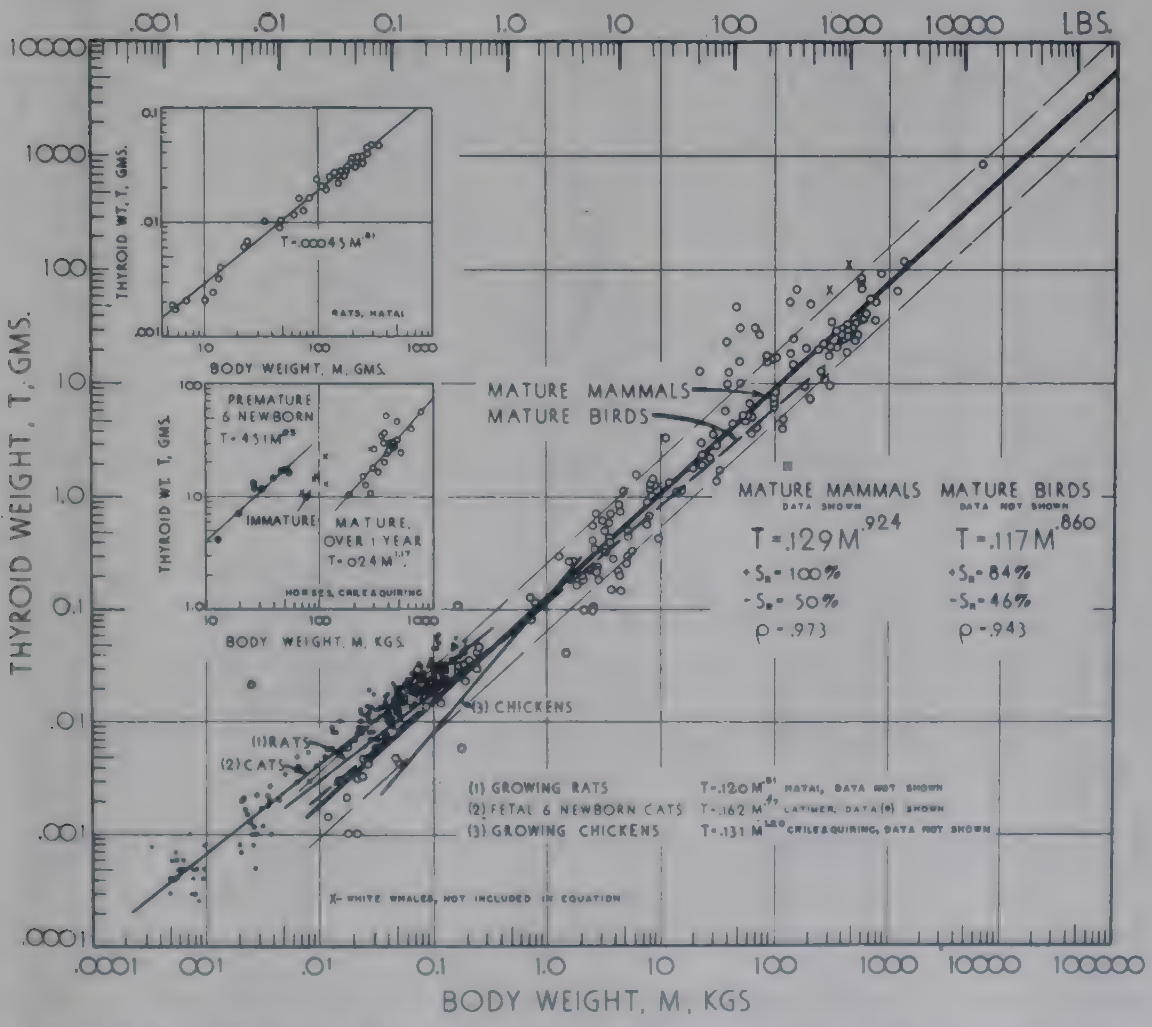

Fig. 17.29a. Thyroid weight in different species (Brody and Kibler, *l.c.*).

It may be so. It is known that the blood supply to the brain—about 13 per cent of the cardiac output (Barcroft and others)—is all out of proportion to the relative weight of the brain. Kestner[31] estimated that under *basal metabolism* conditions nearly half of the blood passes through the brain. Hence Kestner's conclusion that under basal metabolism conditions the brain probably conditions the level of basal metabolism.

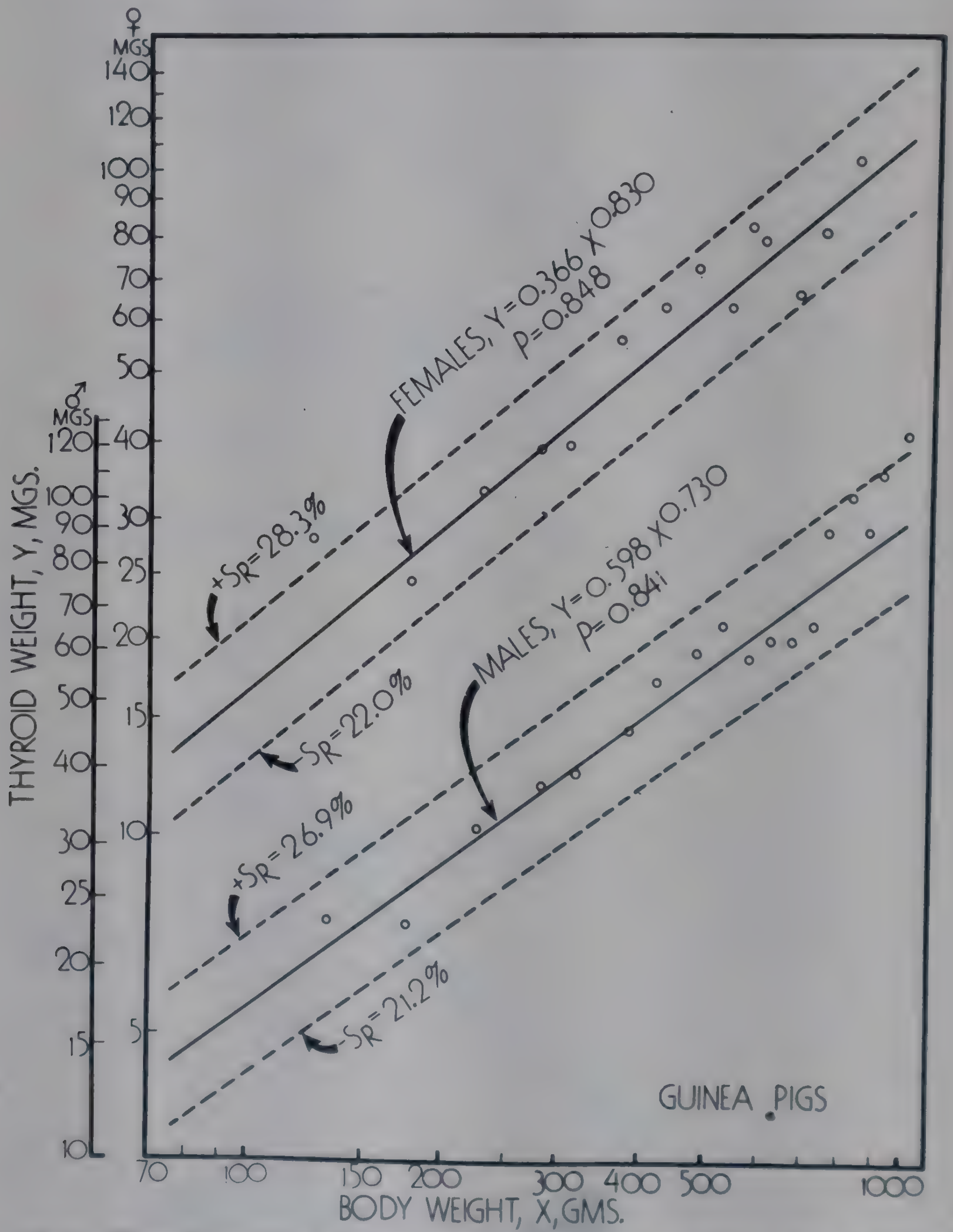

Fig. 17.29b. Thyroid weight in guinea pigs (Mixner, Bergman, and Turner *l.c.*).

Crile[32] emphasized the metabolic importance of the brain: "The brain is the universal executive of energy and is adaptively controlled by the thyroid glands for its constant energy and by the adrenal gland for its emergency energy. Throughout the animal kingdom the primary role of the brain is to maintain body temperature and to drive the muscles and organs in attack and escape. It is the function of the brain alone to execute the oxidation for the long and short swings of both the thyroid and the adrenal glands. We found that it requires 1 gram of brain to execute 12.115 Calories in twenty-four hours."

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[31] Kestner, O., *Proc. Physiol. Soc.* (1935), in *J. Physiol.*, **87**, (1936).

[32] Crile, G., "A neuro-endocrine formula for civilized man." Reprint from "The Educational Record Supplement" for Jan. 1941, Am. Council Education, Washington, D. C.

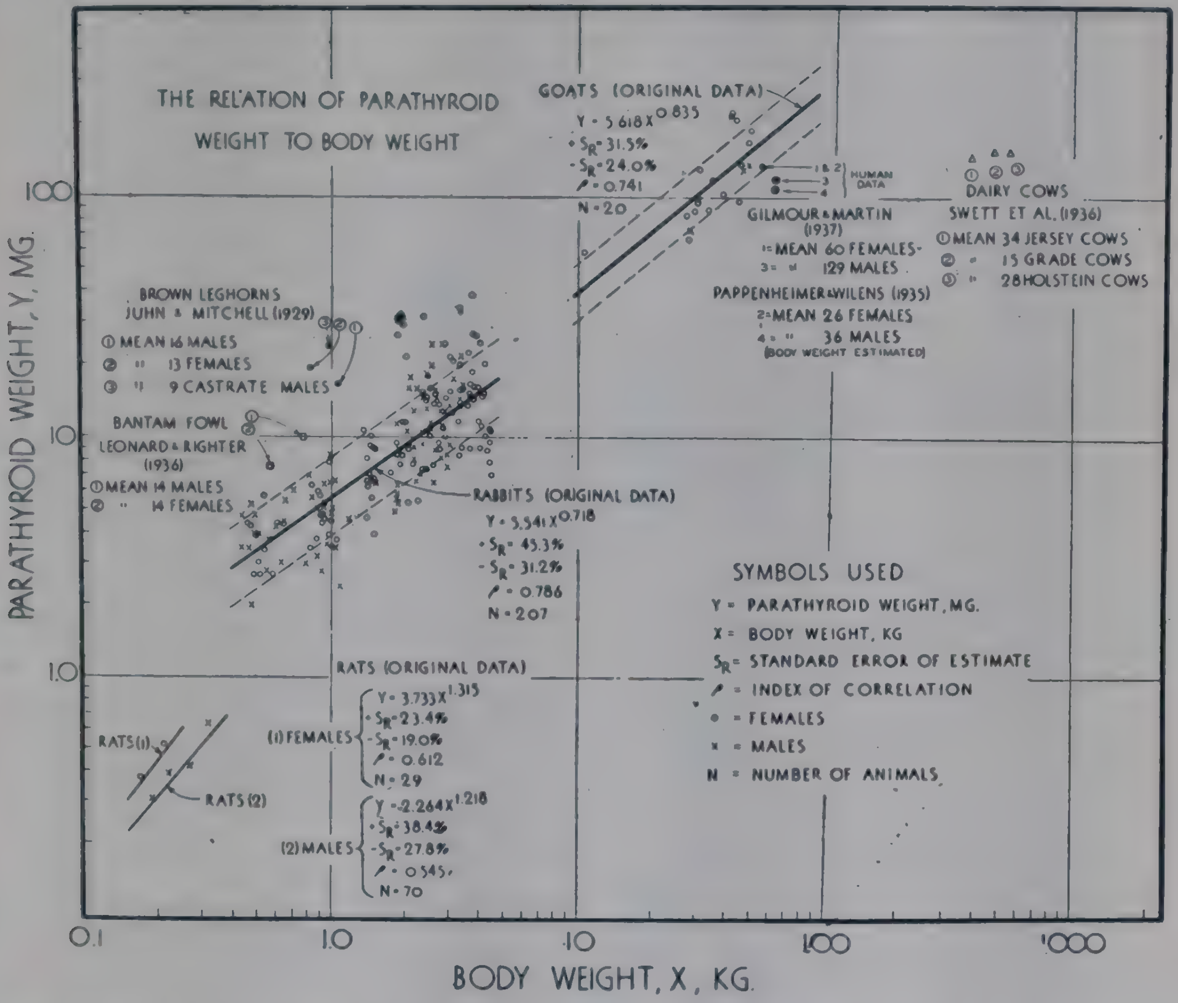

Fig. 17.30a. Parathyroid as function of body weight, by Campbell, I. L., and Turner, C. W., Mo. Agr. Exp. Sta. Res. Bull. 352, 1942.

The influence of environmental temperature, and consequently of the level of heat production, on size of brain was demonstrated in a spectacular manner by Crile and Quiring[33] on two animals of the same weight, namely a 521-kilogram horse and a 521-kilogram White or Beluga Whale. The total daily heat production must be greater in the whale than in the horse, because sea water conducts heat 27 times as rapidly as air, and moreover the water in which the whale lives is below 0°C, much lower than the average air temperature in which the horse lives. The whale, generating more heat than the horse, has a brain 2.9 times and a thyroid 3.2 times larger than the horse. Hence the casual relation of brain and thyroid to heat production, and the conclusion that certain of the visceral organs, especially the brain, are "energy activators".[34] However, while the human brain is the largest, 10-fold the size in a sheep of the same body weight, yet the basal metabolism of man is less than of a sheep.

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[33] Crile, G., and Quiring, D. P., "The energy releasing organs of the white whale and the thoroughbred horse 'Equipoise'," *Growth*, **4**, 291 (1940).

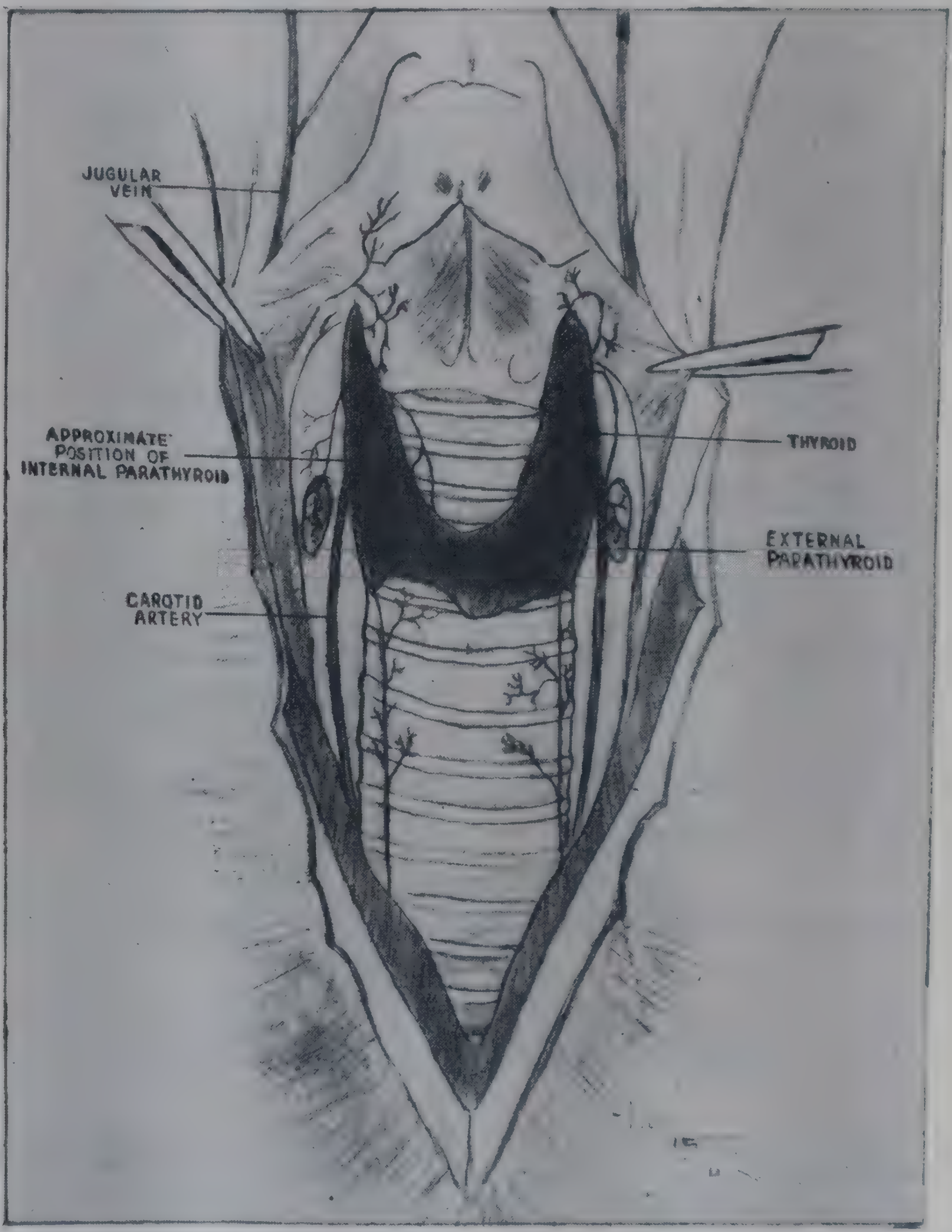

Fig. 17.30b. Location of parathyroids in the rabbit, by Campbell and Turner, *l.c.*

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[34] The following table from Crile illustrates the influence of environmental temperature on *relative* weight of brain, thyroids, adrenals, and the heart.

	"Relative Size"			
Animal group	Brain	Thyroids	Adrenals	Heart
Tropical rodents	.10	.09	.44	.11
Northern rodents	.13	.20	.72	.13
Tropical carnivors	.39	.43	.38	.25
Northern carnivors	.61	.60	.29	.44
Tropical ungulates	.65	.41	.29	.36
Northern ungulates	.70	.43	.29	.52
Cetacea	2.30	1.60	.37	.37

We next discuss charts relating individual organs to total body weight. All the charts are on logarithmic paper; the mature *mammals of different species* are represented by heavy continuous lines, the mature *birds of different species* by heavy broken lines; the animals of the *same species* of different weight, growing or mature, by lighter continuous curves labelled (GR). The very light broken lines on each side of the heavy continuous lines (for mature mammals of different species) represent the standard errors of estimate, *Sr*, which include between them two-thirds of the data points. The average line represents $Y = aX^b$ fitted to the data by the method of least squares. The constant *rho*, the index of correlation, has the same significance for these curves as the constant *r*, the coefficient of correlation, for linearly related data. The given data points (circles except where otherwise indicated for a special reason) represent mature animals of different species only. (The data points for the birds and growing animals of the same species are omitted in the interest of legibility.) Each of the data points is the average of a number of animals. The number and sources of data are listed in the appendix.

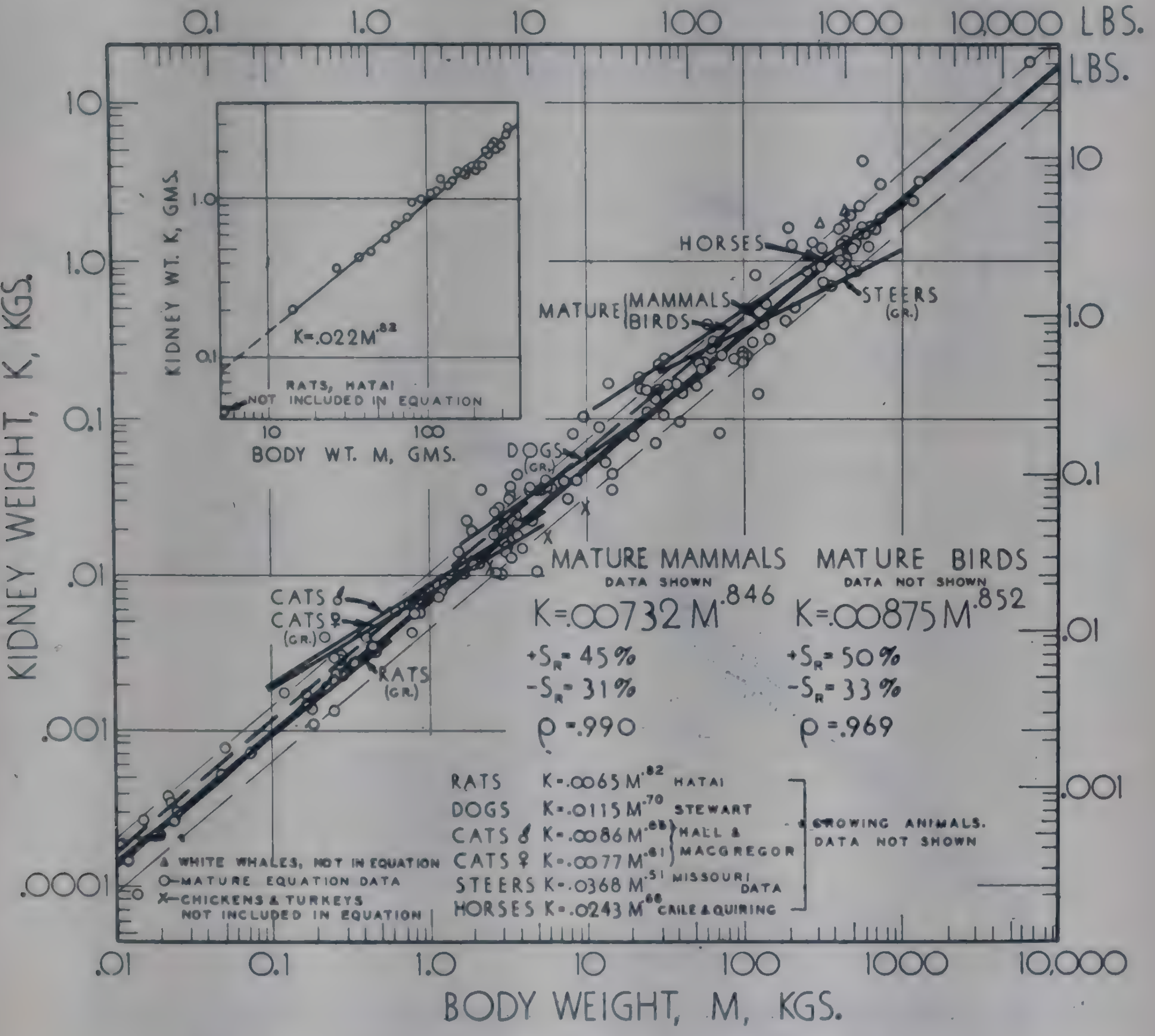

Fig. 17.31. Kidney weight. See also Fig. 17.5e (page 589).

The "prediction" values (computed from the fitted equations) for organ weight corresponding to given body weight are also given in the appendix.

Brain weight: There are more data on the weight of the brain than on any other organ because of its human interest. Fig. 17.8a presents some of the available data on the relation of brain weight to body weight plotted on logarithmic paper (see also Fig. 10.1).

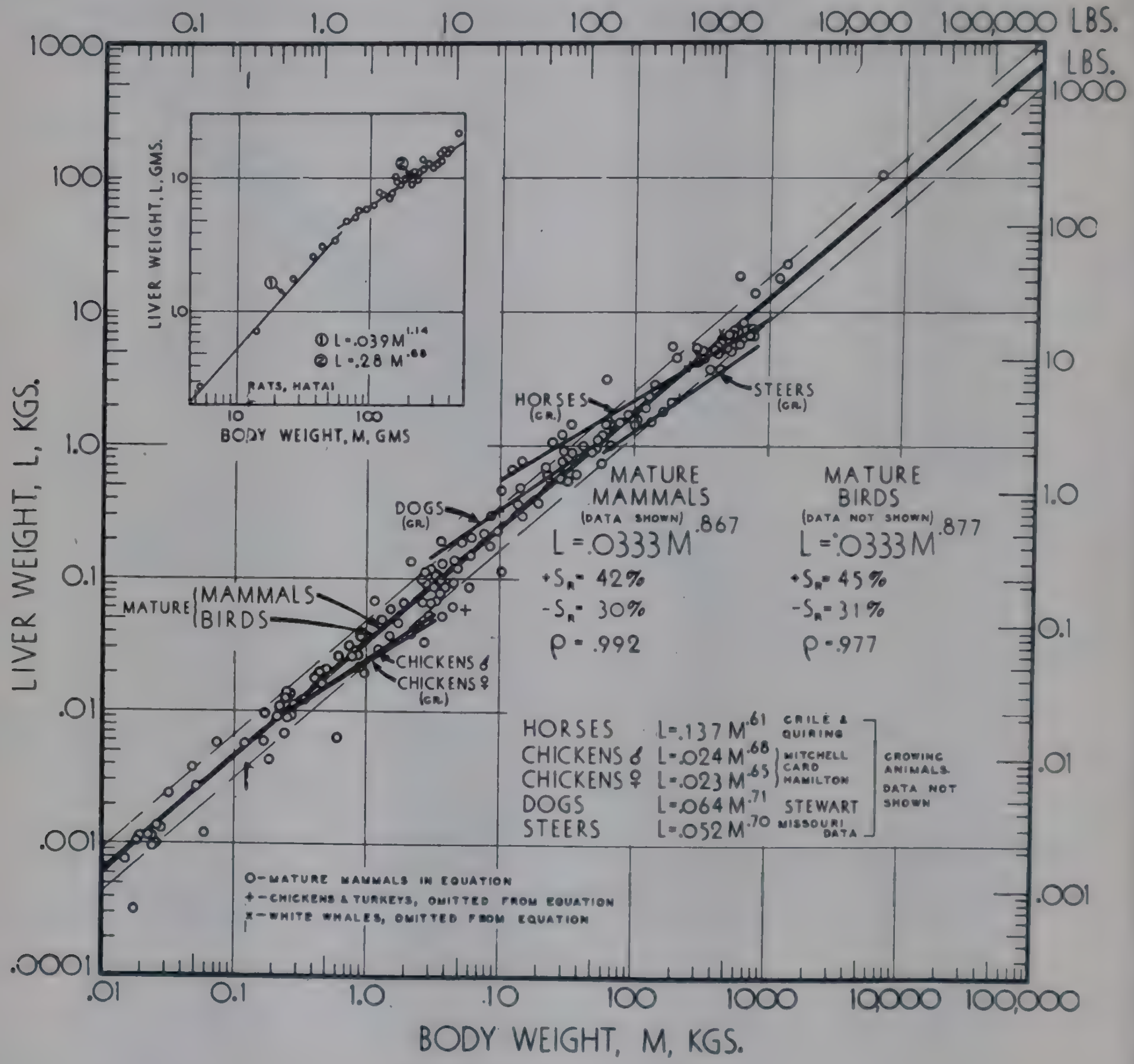

Fig. 17.32. Liver weight.

As previously noted, the brain weight in mature mammals of *different species* varies with approximately the 0.70 power; that is, doubling body weight increases brain weight about 70 per cent. The values of $+Sr$ and $-Sr$ indicate that two-thirds of the data fall between $+64$ and -39 per cent of the average curve. The index of correlation, which is 0.97, is very satisfactory. The value of the exponent for birds is considerably less than for mammals, meaning that, in comparison to small birds, large birds have relatively smaller brains than mammals.

The other curves and equations in Fig. 17.8a represent the brain-body relations of animals in various stages of growth. Except for the early stages of growth (see the 1 to 15-day interval post-natal growth in the rat, in the upper-left insert chart), the slopes of these curves (for animals of the same species) are usually very much lower than for mature animals of different species, the exact values depending on the period of growth. The later the period of growth, the lower is the slope. In general, as noted by Du Bois and Lapicque, the post-natal slope relating brain to body in the same species is near 0.25.

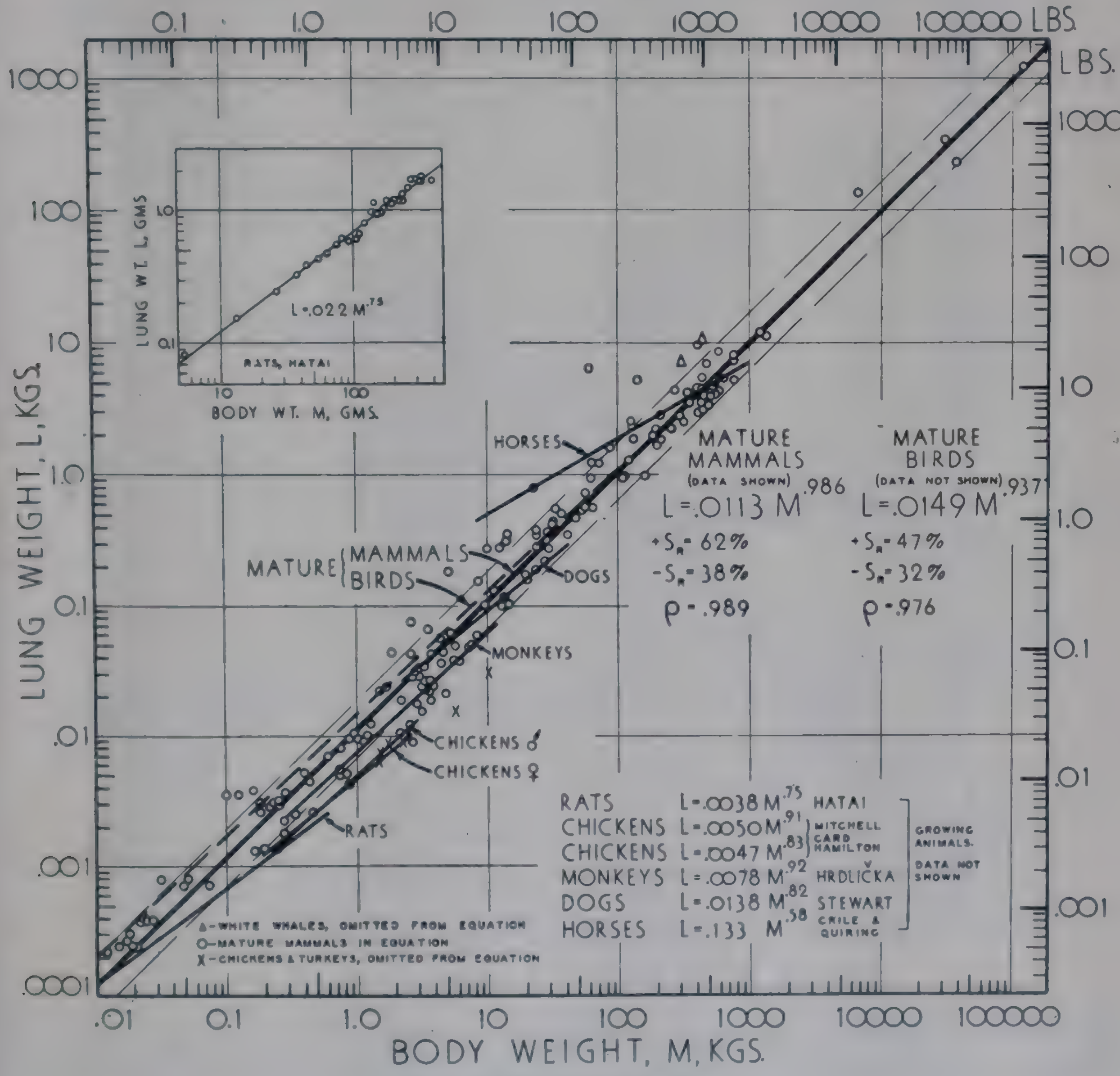

Fig. 17.33. Lung weight.

Note that the brain weights of small whales (triangles), of Simians (X's), and especially of man (black circles), are very much above the average line, whereas those of large whales are below the average. These species were not included in computing the equation represented by the curves.

Summarizing for mature animals of different species, the slope of the curve relating brain weight to body weight parallels the slope of the curve relating basal metabolism to body weight. The values of slopes relating brain weight to body weight in growing animals of the same species depend on the growth period; the younger the animal the steeper the slope. During the later periods of growth, for which most data are available, the slopes are very much below those for mature animals of different species.

Pituitary weight: Few data are available on the pituitary weight. Because of the importance of this organ, the few available data are charted in Figs. 17.9a, b, and c. It appears that the slope relating pituitary weight to body weight in mature animals of different species, 0.76, is quite close to the slope of the curve relating basal metabolism to body weight, 0.73. The slope is somewhat less for post-natally growing animals within the species.

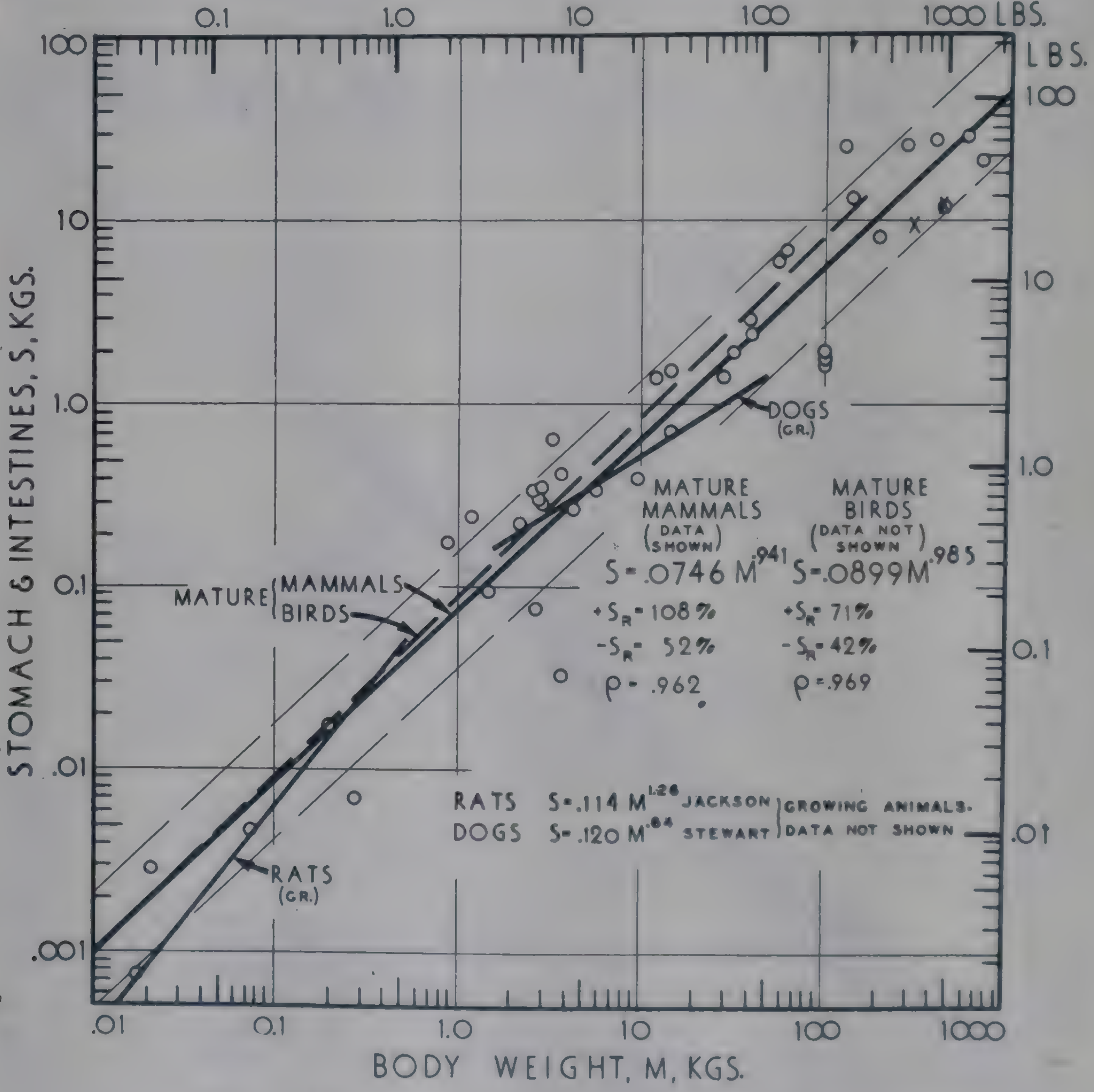

Fig. 17.34. Stomach and intestine weight.

As with brain weight, age is an important factor conditioning the slope of the pituitary curve of animals of the same species.

Heart weight: As previously indicated, the metabolic level depends on the interrelation of several systems, including the stimulating or afferent (neuro-endocrine) system, and the receptive or efferent (cardiovascular) or operating systems. The brain and pituitary discussed above exemplify the stimulative system; the heart discussed in this section exemplifies the receptive or operating system.

The heart weight is correlated with the exercise level of the species and individual. This is illustrated in Fig. 17.10. Aquatic animals invariably have relatively smaller hearts than terrestrial animals because their weight is counterpoised by the weight of the water they displace; they are not obliged

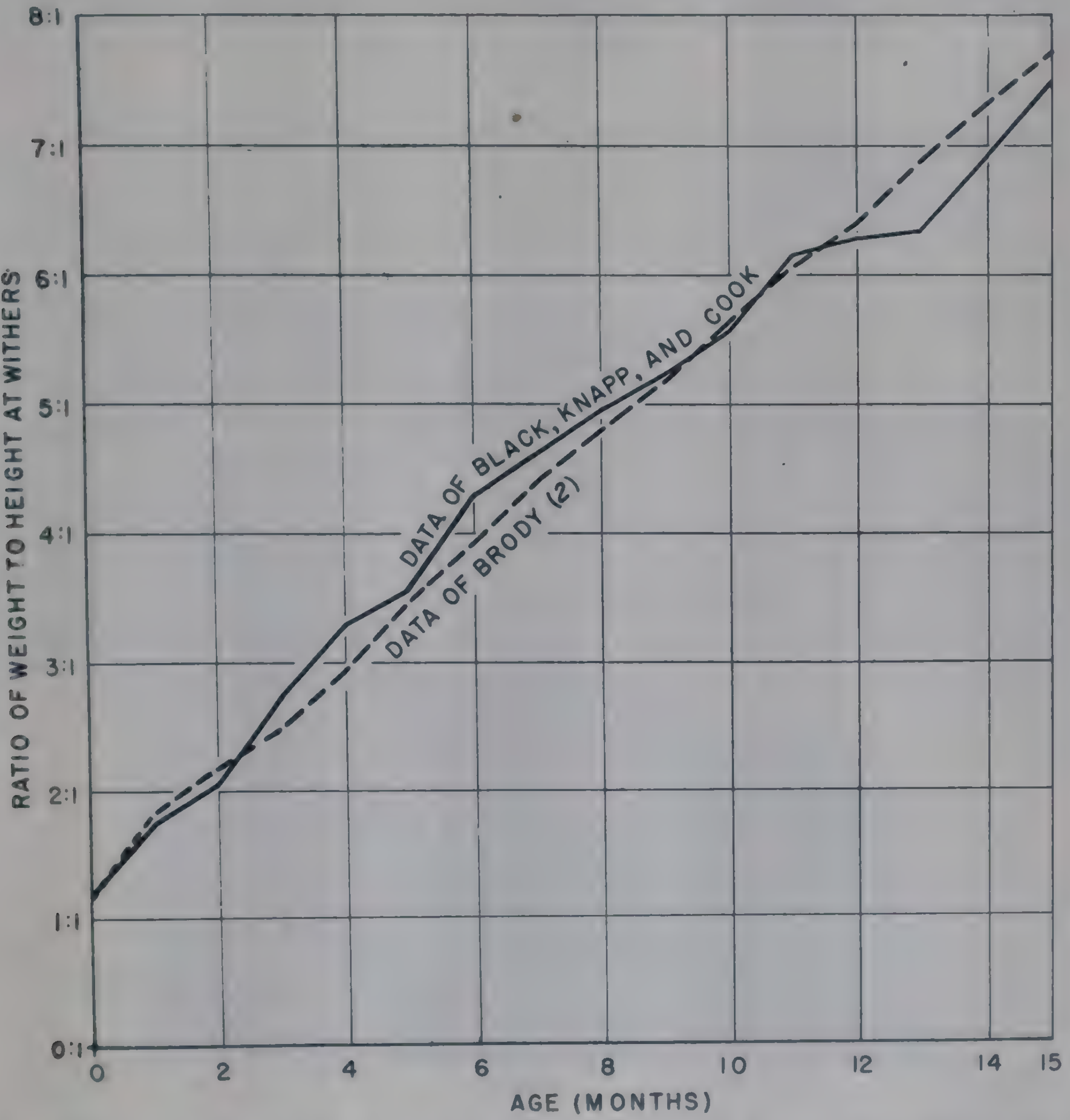

Fig. 17.35a. It is shown in Fig. 17.1c that body weight is very sensitive to food supply, chest girth is less sensitive to food supply, and height at withers in cattle is virtually unaffected by food supply. Hence height at withers is the best index of the genetic size of the animal, independent of food supply. Fig. 17.35a by W. H. Black, B. Knapp, Jr., and A. C. Cook [*J. Agr. Res.*, **56,** 465 (1938)] brings out the same idea in a different way: the ratio of weight to height at withers gives the highest correlation with "performance" (gain in weight). Fig. 17.35b brings out the same idea in a still different way: 50 per cent of height at withers (measurement *1) is completed before birth as contrasted to 6 per cent of body weight. Hence food supply does not have the opportunity to affect height at withers (measurement *1) as it can weight or chest girth (*18, see Table 1) the second most easily measured linear dimension. While 17.35b shows percentage of mature size at birth, Fig. 17.35c shows multiples of birth size. Thus hip width at 5 years (virtual maturity) is 3.3 times or 330 per cent times the heart girth at birth. These 3 charts are for cattle.

to overcome the pull of gravity, as are terrestrial animals which must mak successive liftings of the body against gravity when walking or running Likewise, terrestrial animals, known for their running ability, such as horse and dogs, have relatively larger hearts than domestic pigs or guinea pigs.

Similarly, as might be expected, the heart weight tends to vary mor directly with body weight (rather than with basal metabolism) during growt than would other visceral organs, such as the neuro-endocrine, because th work performed by the heart in walking varies directly with the body weight

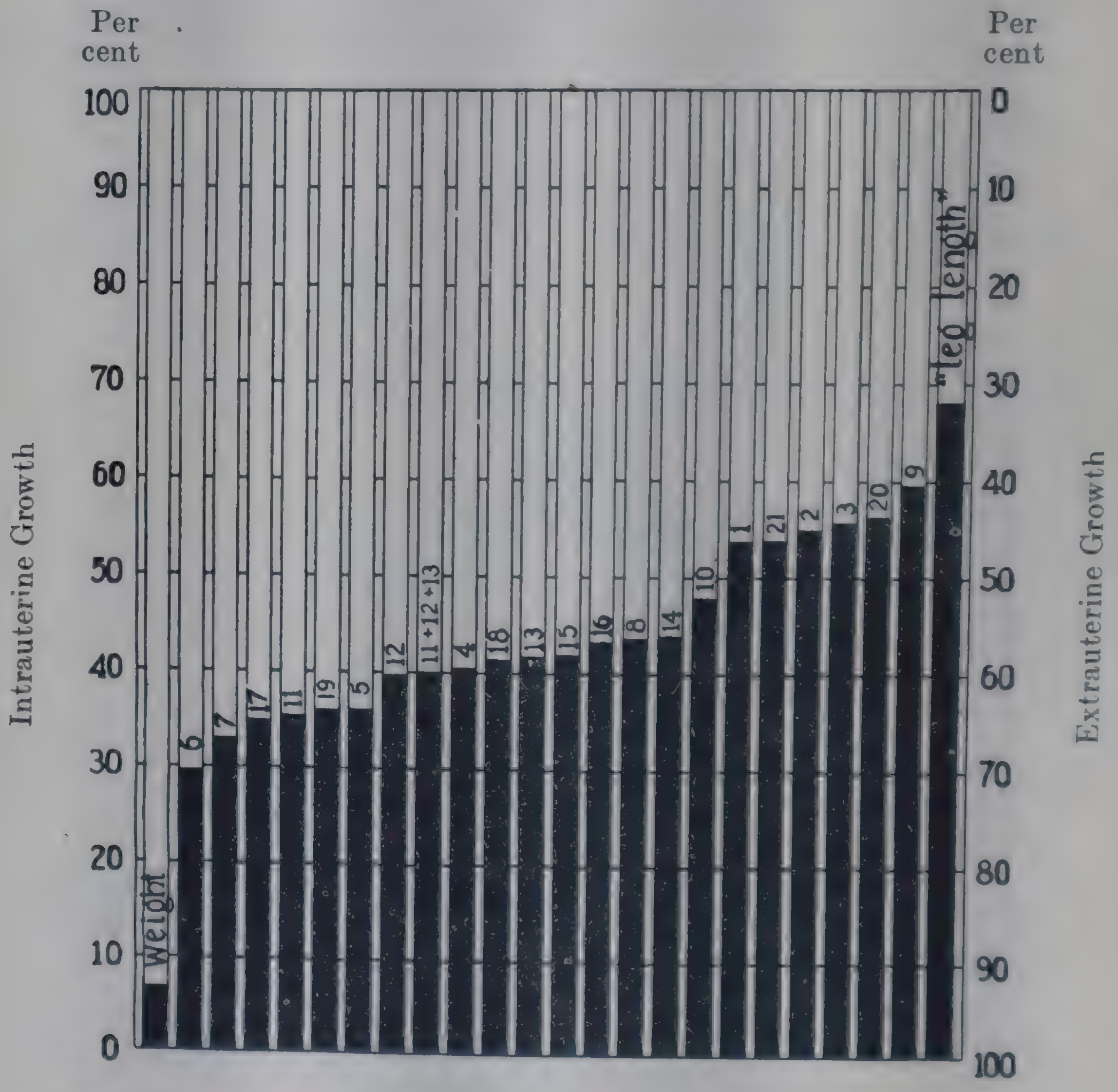

Fig. 17.35b. See caption for Fig. 17.35a; also Fig. 17.11 and Table 17.7.

In other words, the slope, b, of the curves relating heart weight to bod weight is in many cases very close to unity, as shown in Fig. 17.10; still, especially as shown in the insert on the upper-left corner of Fig. 17.10b, it i much better to relate heart weight to body weight by the power equatio $Y = aX^b$, than by the linear equation $Y = a + bX$.

Other visceral organs: The foregoing discussions of the typical viscera organs—brain, pituitary and heart—are applicable, with slight variations, t practically all other visceral organs. The charts for the other visceral orga in relation to body weight are therefore presented in the appendix without much discussion.

To summarize, the slope relating metabolism to body weight parallels the slope relating the weight of some neuro-endocrine organs to body weight. The weight of the heart, on the other hand, tends to vary more directly with body weight (slope near unity) as the work performed by the heart in locomotion tends to vary directly with body weight. For direct agricultural applications concerning the relation of muscular and fat tissues to visceral tissues, see Hammond[9] and text books on stock judging.

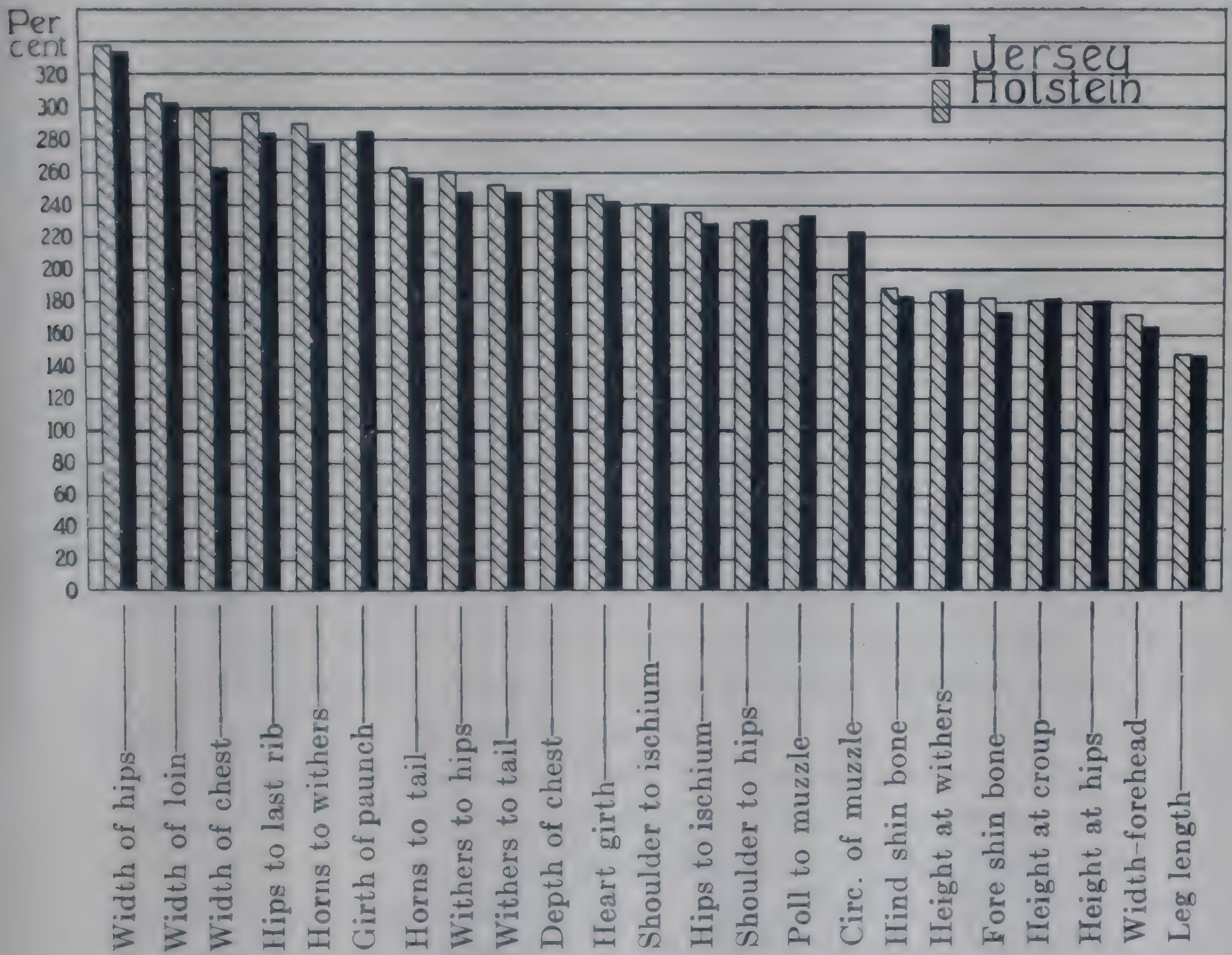

Fig. 17.35c. See caption for Fig. 17.35a, b.

17.5: Linear growth and form. Age change in form is, of course, associated with differences in growth rates in different directions. As explained in the preceding section and illustrated by Figs. 17.1a to d, change in form may be observed (1) *qualitatively* by comparing outlines or photographs of the animal at different ages; (2) *semi-quantitatively* by comparing the slopes of the age curves of growth in various directions, and (3) *quantitatively* by fitting the relative-growth equation, that is, the parabola $Y = aX^b$, to the data after first plotting Y against X on a log-log grid and noting the nature of distribution of the data.

While the age curve of growth in weight describes the change in the *organism as a whole*, the age curve of growth of some one linear dimension describes the change in only one of many linear measurements, which may or may not be proportional to the change in other linear measurements or to the change in weight. Thus (Fig. 17.1c) the post-natal growth of the rabbit cranium is no index of the post-natal growth of other linear measurements or of the body as a whole, for all the photographs were reduced to the same cranium size.

The same may be said with regard to several other comparative outlines in Fig. 17.1. In other words, higher animals grow not in one, two, or three different linear dimensions, but in many. The concept of n-dimensional change is now generally understood. This, of course, is the reason why weight cannot be expressed exactly as the cube of some *one* linear measurement, or that surface area cannot be represented as the square of some *one* linear measurement, or even as the $\frac{2}{3}$ power of weight, which represents all the n-linear dimensions and which should, therefore, be something of an average.

Then too, weight (volume) growth prior to puberty tends to be self-accelerating, that is, to grow in a *geometric* progression (one cell giving rise to 2, 2 to 4, 4 to 8, 8 to 16, etc.) and to plot linearly against age on *arithlog* paper, at least for short periods, whereas linear growth, *i.e.*, terminal growth, tends to grow in an *arithmetic* progression, according to the series 1, 2, 3, 4, etc., and to plot linearly on arithmetic paper. There is an inflection in both cases, but the inflection is likely to occur at different ages, for example, earlier for the length of the rabbit cranium than for the length of the rest of the body (Fig. 17.1c), and still earlier than for the total body weight.

17.5.1: Age curve of linear growth. In view of the nature of linear growth, complicated by the fact that there is not one but n linear dimensions, each growing at a rate different from the others, it seems desirable to examine a few linear age curves of growth before proceeding with the fitting of the parabola to the relation of linear size to weight.

Most of this analysis relates to dairy cattle measured at the Missouri Station by Eckles, Ragsdale, and associates[35] and at the Nebraska Station by Davis, Morgan, and associates.[36] The data on man are from the literature.

Fig. 17.11 shows the measurements taken and the numbers by which they are referred in the text. Table 17.7 names each of the measurements and gives the numerical values of the constant A (mature size), $100k$ (percentage decline in growth rate per month), and the ages at which various fractions of A are attained (see Ch. 16 for details).

Tables 17.8 and 17.9 give the numerical values of the measurements plotted in Figs. 17.12a and b. The agreement between observed and computed values is satisfactory for each of the linear measurements growing at a different relative rate ($100k$) from every other linear measurement. The exponential equation $L = A - Be^{-kt}$ (Ch. 16) may thus be said to represent the "ground plan" of the later linear growth, as indeed of weight growth.

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[35] Brody, S., and Ragsdale, A. C., Univ. Mo. Agr. Exp. Sta. Res. Bulls., 80, 89, and (with H. P. Davis) 262.

[36] Davis, H. P., Morgan, R. F., Brody and Ragsdale, Univ. Neb. Agr. Exp. Sta. Res. Bull., 91, 1937.

Fig. 17.13 shows that this equation also represents linear growth in man following puberty. While the maximum height, A, ranges from 153 to 172 cm, and the value of $100k$ ranges from 45 to 82 for the various groups, they may all be represented by the same equation, $L = A - Be^{-kt}$; they all have the same basic growth plan.

So much for the later (self-inhibiting) phase of linear growth.

Now as regards the earlier phase, prior to the inflection, Fig. 17.14a shows that in cattle, when weight growth has an increasing slope (geometric progression) on arithmetic paper, linear growth has a constant slope (arithmetic progression). Fig. 17.14b shows a similar situation for the growth of man.

Summarizing, in early life when weight growth tends to occur in a geometric progression, or exponentially, linear growth tends to occur in an arithmetic progression, or linearly. Following puberty, both weight and linear growth decline exponentially, as indicated by the excellent fit of the equation $L = A - Be^{-kt}$ to the data.

17.5.2: Relation between linear and weight growth. As previously explained, the applicability of the parabola $Y = aX^b$ is determined by plotting Y against X on a log-log grid, and estimating the value of b by measuring the slope of the line drawn through the data by inspection; or if desired, this equation may be fitted to the data by the method of least squares (Ch. 13). Figs. 17.15 to 17.18 represent weight plotted against some linear size with the slope, b, estimated by inspection. Note from Fig. 17.15 that the distribution is linear on the log-log grid[37], indicating that the parabola fits the data. Figs. 17.16 to 17.18 illustrate how such data appear when plotted on arithmetic paper. Here the curve rises as expected from the fact that weight growth tends to vary with the cube (third power) of linear growth. However, as indicated by the equation, the slope is not 3, but it ranges from 2 for the relation of weight to width of hips, 3 for the relation of weight to chest girth, and 4 for the relation of weight to height at withers. The chest girth thus comes nearest to being the theoretical average of linear growth—to meeting the dimensional-analysis expectation that weight varies with the cube of linear size.

While the distribution of the weight to linear size data appears to be uneventfully smooth in Figs. 17.16 to 17.18, if the ratios weight/(linear size)^b are plotted against age, as shown in Fig. 17.19, with the corresponding values of the exponent b given in Figs. 17.16 to 17.18, the resulting curve shows systematic variations. This substantiates what was previously said about the capacity of the parabola $Y = aX^b$ to swallow up in the general trend small though significant differences in rate and method of growth.

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[37] Fig. 17.15 from Ragsdale, A. C., Regan, M. J., and Brody, S., Univ. Mo. Agr. Exp. Sta. Res. Bull., 142, p. 13, 1930. The other charts plotted from Tables 17.8 10 and 17.15.

What was said about the relative-rate of growth of cattle probably holds true of other grazing animals, for example, horses, as indicated in Fig. 17.20. The numerical values of the slope, b, for growing horses is nearly the same as for growing cattle.

The relative-rate of growth of humans shows an opposite extreme as illustrated in Figs. 17.21 and 17.22. The relation of weight to height in humans shows conspicuous breaks in the curve at 1, 5, and 15 years, the last two ages corresponding to the beginning and end of the juvenile period, and the first the end of the exclusive dependence on milk. (Compare with Figs. 16.7, 16.50, 16.52 and especially 17.1e.) Moreover, proportional growth at different ages in humans is in many respects different from that in horses and/or cattle. Thus in humans, leg length is relatively slow prenatally and most rapid during the juvenile period (Fig. 17.1); in cattle and horses, practically all the leg-length growth is completed before birth. The parabola does not, therefore, represent the relation of weight to linearly measured complexes as satisfactorily in humans as it does in cattle and horses, but it is the best equation available for analytic as well as predictive purposes, which we consider next.

17.6: Estimating weight of cattle from chest girth. Dairymen do not often have scales for weighing cattle; yet weight is very important for estimating feed needs, energetic efficiency, and monetary profit from milk production (Ch. 22) and growth. The apparently satisfactory applicability of the parabola $Y = aX^b$ to the relation of weight to chest girth (Figs. 17.15, 17.16, 17.23, 17.24) suggested the idea of employing the equation for predicting weight from chest girth[38]. Accordingly, this parabola was fitted, by the method of least squares, to 15,610 pairs of body-weight and chest-girth measurements of dairy cattle of all ages owned by the Missouri and Nebraska agricultural experiment stations,[35, 36] with the results shown graphically in Fig. 17.23.

The heavy line represents the fitted parabola; the light broken lines, the standard errors of estimate, $+Sr$ and $-Sr$, between which are included two-thirds of the data. The constant, ρ, for the logarithmic relation corresponds to the coefficient of correlation, r, for arithmetical relations.

All the curves in Fig. 17.23 were brought together for purposes of comparison in Fig. 17.24. The outside broken lines represent the standard error of estimate of all the data.

Figs. 17.23 and 17.24, which include 15,610 weight-chest measurements, represent 6 sets of data: 2454 measurements on Missouri Holstein cattle; 2235 Missouri Jerseys; 5866 Nebraska Holsteins; 2758 Nebraska Jerseys;

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[38] The chest girth is easily measured by placing the tape about 6 inches back of the front legs.

840 Nebraska Guernseys; and 1457 Nebraska Ayrshires. A close examination of the curves in Fig. 17.24 indicates that during the earlier periods, the Nebraska cattle, particularly the Holsteins, are heavier for a given chest girth than the Missouri. This difference is attributed to the higher nutritional level of the Nebraska calves and to the greater influence of a high nutritive level on weight than on chest girth. While the difference is significant statistically, it is probably not so practically.

For purposes of comparing the degree of agreement between observed and computed weights, "observed" weights were obtained by grouping the chest-girth values into 1-inch intervals, *disregarding age*, and computing the geometric means[39] of the weights for these 1-inch chest-girth intervals. These "observed" means are compared in Table 17.10 to those computed from the fitted parabola.

An attempt was made to improve the predictive values of chest girth by sorting the data by ages into month intervals, then relating weight to chest girth for each month separately. The results are shown in Tables 17.11 to 17.14 in the appendix.

While including age in the prediction table improves the prediction value of the chart, the following shortcomings of the age-girth-weight prediction charts may be pointed out:

(1) Dividing the data by age classes reduces the number of data in each class, and consequently reduces the regularity of distribution of the data.

(2) As a result of (1), the fit of the parabola $Y = aX^b$ to data and its prediction values become less certain.

(3) The numerical value of b of the parabola, when thus fitted to the reduced data, is not near 3, as found when the data are grouped by chest girth regardless of age, but is near 2, a result which is very disturbing from the viewpoint of dimensional analysis, and suggests further investigation.

(4) Difference in feed supply probably affects predictions obtained on the basis of age classes to a different extent than when age is overlooked. This problem obviously calls for further intensive study.

From the above considerations it is not safe to advise which method of prediction should be used, that in Table 17.10, ignoring age, or that in Tables 17.11 to 17.14, including age. The dairyman will simply have to check each of the tables on the animals in his herd, and use the ones which give best agreement with his own measurements.

The use of Table 17.10 for prediction is simple: measure the chest girth and read the weight from the column representing a given breed, or from the grand average. This is perhaps the best method, although no doubt special gadgets, slide rules, etc. may be devised for this purpose. There is need for a good tape measure, one which will withstand the rough handling without stretching, shrinking, curling, and breaking.

To estimate weight from Tables 17.11 to 17.14, measure chest girth, note the age of animal, and read the weight corresponding to the given chest girth and age. The bold-face values represent the averages of the measured animals.

The following are additional comments in favor of employing chest girth and the logarithmic equation for predicting weight:

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[39] There is no practical difference between *geometric* and *arithmetic* means for the given narrow chest-girth intervals. The geometric means are probably theoretically superior to the arithmetic means because of the geometric or logarithmic relation between weight and chest girth.

(1) From the viewpoint of dimensional analysis, chest girth comes nearest to being representative of the linear size of the animal as a whole because the numerical value of the exponent b in the parabola is nearest to 3. This means also that weight growth is most closely correlated with chest-girth growth.

(2) If the ratio weight/(chest girth)^b is plotted against age, as shown in Fig. 17.25, it does not exhibit the same consistently systematic deviation from the average in all groups. The fact that the trends vary from group to group indicates that they are probably caused by management (feeding) conditions. Thus the Nebraska curves show high, and the Missouri curves low initial ratios. The group differences in weight at given chest girth levels indicate that the relation between weight and chest girth is in part dependent on nutritive condition: a relatively high nutritive level at the early ages causes a relatively (with regard to the equation level) greater weight increase than chest-girth increase, presumably because of relatively greater weight deposition in other regions than around the chest.

(3) While the precision of the measurements is arithmetic, that of the fit of the equation is logarithmic. Now it can be shown that in the equation $Y = aX^b$ and its logarithmic form $\log Y = \log a + b \log X$ the precision of $\log Y$ is Y times the precision of Y; therefore the predictive reliability is better when employing a logarithmic equation fitted logarithmically, as was done in this section, than when employing an arithmetic equation fitted arithmetically.

(4) It may be noted, as is generally known, that weight measurements, Y, can be made with greater precision than linear measurements, X. Account should be taken of these differences in precision of measurements in fitting the equation;[40] this was not done. However, of all the linear measurements taken of cattle, those of chest girth probably involve least error, and therefore give best predictions for body weight.

Summarizing, this section presents an important practical application of the parabola $Y = aX^b$: a vast body of data (15,610 animals) representing four breeds of cattle of all ages and conditions at the Missouri and Nebraska Stations were welded together by this parabola for the purpose of preparing a thoroughly representative and reliable table for estimating weight from chest girth of dairy cattle of unknown (Table 17.10) or known (Tables 17.11 to 17.14) ages. Statistical analysis indicates that changes in chest girth and weight in cattle are particularly well correlated, and that when using the average curve in Table 17.10, two-thirds of the prediction over the whole range of data may be expected to fall within ± 13 per cent of the average. Theoretically, closer prediction may be expected if the breed prediction table is employed, and still closer if the breed-age-chest girth-weight tables (17.11 to 17.14) are employed. Of all the linear measurements investigated, chest girth in growing cattle appears to be most closely correlated with body weight, and is most nearly representative of the linear size of the animal. This is indicated by the fact that weight varies most nearly with the cube of chest girth. This means that an increase in chest girth by 1 per cent is associated with an approximately 3 per cent increase in body weight.

17.7: Estimating nutritive condition of cattle from height at withers. Nutritive condition in the sense of underweight or overweight is an important factor in the efficiency complex (Ch. 5). It is, therefore, important to have a method for measuring the nutritive condition of an animal in comparison to a standard, for example, the average condition of cattle of the breed.

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[40] Deming, W. E., U. S. Bureau of the Census, Washington, D. C., Personal communication.

It was demonstrated in the preceding section that chest girth is one of the linearly measured complexes most closely correlated with body weight. Height at withers, on the other hand, is one of the measurements least correlated with body weight. This is demonstrated in Fig. 17.1b, in which the weights, chest girths, and heights at withers are plotted against age on arithlog paper. At age 3 years, the weight of the full-fed group I is over twice that of the underfed group II; the chest girth of the full-fed group I is correspondingly greater than of the underfed group II; but the height at withers of both groups of cattle is virtually the same. Height at withers in cattle is not easily influenced by nutritional conditions, partly because over half of this linearly measured complex is completed by the time the animal is born.

It therefore seemed that height at withers would make an ideal reference base for estimating the degree of fleshiness of an animal in comparison to her own ideal size, or at least in comparison to the average animal of her breed. Thus, if a given Holstein having a height at withers of 52 inches weighs 1100 pounds, and the ideal Holstein (of the same age if possible) weighs 1000 pounds, the given animal is 100 pounds, or 10 per cent, overweight.

The problem of this section is to weld together a large body of data on the relation of weight to height at withers with the aid of the parabola $Y = aX^b$ in the same manner as was done in the preceding section on the relation of weight to chest girth, employing the same animals. The results are shown in Fig. 17.26. The corresponding numerical predictions relating weight to height, without reference to age are given in Table 17.15. The predictions of weight to height at withers including the age factor are given in Tables 17.16 to 17.19. These tables are based on the Nebraska data. The Missouri and Nebraska data do not agree as well for this height-at-withers relation as for chest girth. This very disagreement testifies to the sensitiveness of height at withers as a reference base for estimating the nutritive state of cattle. The two stations feed the animals on somewhat different planes, with consequent differences in the ratios.

Summarizing, this section presents another practical application of the parabola $Y = aX^b$, namely for predicting nutritive condition from height at withers of cattle. The weight of growing cattle varies not with the cube of linear size, as was previously found for the relation of weight to chest girth, but more nearly with the fourth (4.3) power. This means that increasing height at withers by 1 per cent tends to increase body weight by approximately 4 per cent. In other words, height at withers in growing cattle is very much less influenced by increase in body weight than is chest girth. This fact is illustrated in several ways in the text. The fit of the parabola $Y = aX^b$ is not as satisfactory in relating weight to height at withers as it is in relating weight to chest girth.

17.8: Note on the relation of weight to height in humans. Because the growth curves of humans are more complicated and variable than of cattle, the method of assessing body build and nutritional status of cattle is not satisfactory for humans.

Many indices of body build and of nutritional status of children have been published.[41] In Europe one usually hears of the "baric index",[42] which is 100 times the ratio of weight to the cube of height (100 × weight/height^3), or what is equivalent, the "ponderal index", 100 × weight$^{\frac{1}{3}}$/height.

As previously explained, weight rises with the cube of linear size, or the cube root of weight rises with the linear size in geometrically similar bodies, which human bodies are not. These indexes do not seem to the writer to be rational.

The common index in this country is weight for given height and age.[43] Davenport[44] suggested that "for young adult males the best index of build is apparently obtained by dividing weight by the square of stature". (Figs. 17.21–2 indicate the reason for the difficulties in finding one overall value of b in the index of build Y/X^b for man.)

Wetzel[45] gave the best expression to the weight-height-age status. The usual three measurements are taken (height, weight, and age), from which Wetzel estimates body build, developmental level, nutritional level, basal heat production, and dietary caloric needs with the aid of his chart. Wetzel's grid is a weight-height surface flanked by a series of isodevelopmental "channels", probably fractions or multiples of the standard error of estimate.

The use of Wetzel's chart involves taking a series of measurements of the same child at least twice, thus considering "the individual child in relation to his own past record of progress". The outstanding feature of Wetzel's method is that it permits estimation of normality of body build by the degree of parallelism of the weight-to-height curve of the given child to the standard weight-to-height curve plotted on a logarithmic grid. The child's nutritional condition progresses normally if his weight-to-height curve parallels the standard, although it may be some distance above or below the standard. The child tends toward obesity or malnutrition if his weight-to-height curve is, respectively, more or less steep than the average. It is, of course, conceivable that the child's curve may parallel the standard, yet be obese or emaciated, when the same degree of obesity or malnutrition is maintained throughout growth. Likewise, a rise or decline in the slope of the weight-to-height curve may represent approach to normal from malnutrition or from obesity, respectively. In other words, this method, like other methods of assessing normality, is a valuable aid to, but not a substitute for, judgment.

Wetzel's grid stresses the idea that children of different body build tend to parallel (rather than to coincide with) the average course of the weight-to-height curve. This idea was stressed by others,[46] but Wetzel's unique contribution is the design of his chart; it brings together the weight, height, age, and also metabolism data into one conveniently designed chart. The weight-to-height zone is divided into seven "physique channels" above and below the standard or middle line, *M*, labelling each line or channel, and explaining that "healthy development continues in an established channel as though this were a preferred path"; in other words, the weight-to-height curve of a normally growing child parallels the standard curve.

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[41] "Report on the work of the group of experts appointed to study methods of assessing the state of nutrition in infants and adolescents," *Bull. Health Org. League Nations*, **6**, 129 (1937). See also, Dublin, L. I., and Gebhart, J. C., "Do height and weight tables identify undernourished children?" New York Assoc. for improving conditions of the poor, 1924. Clark, T., Sydenstricker, E., and Collins, S. D., "Weight and height as an index of nutrition," *Pub. Health Rep.*, **38** (1923). Jenss, Rachel M., and Souther, Susan P., "Methods of assessing physical fitness of children," Children Bureau Pub. 263, Washington, 1940.

[42] *Cf.* Bardeen, C. R., Carnegie Inst. Washington, Pub., 272, p. 483.

[43] See, for example, Baldwin, B. T., *Am. J. Physical Anthropology*, **8,** 1 (1925).

[44] Davenport, C. B., *Am. J. Physical Anthropology*, **3,** 467 (1920); *Am. Statistical Assn. Pub.*, **17,** 341 (1920–1), and "Body build and its inheritance," Carnegie Inst. Wash. Pub. 329, 1923.

[45] Wetzel, N. C., *Jour. Am. Med. Assoc.*, **116,** 1187 (1941). For a critical examination of the Wetzel method, see Hilde Bruch, *Jour. Am. Med. Assoc.*, **118,** 1289 (1942).

The position and slope of a given child's curve below or above the average indicates his relative body build or nutritional level and his trend to average, stock, stout, plump, obese, thin, or slender.

These "physique channels" are connected by lines called "isodevelopmental levels" to a panel on the right side giving a series of "auxodromes" (Greek, course of growth). The body weight and body build or "nutritional" status (weight-to-height) are thus related to chronological age, or to "developmental age"; corresponding to the position, including two-thirds of the children in the given weight class) and also to basal metabolism.

Wetzel notes that the onset of the menarche, which occurs on the average at age 13.6 years,[47] is correlated with "the final deceleration of growth in weight. . .in the neighborhood of the greatest upper curvature".

17.9: Estimating the amount of wool or feathers from body weight. Assuming: (1) that the major function of the body covering of hair, wool, and feathers is the regulation of heat loss from the body; (2) that heat loss is proportional to surface area; and considering that (3) hair and feathers have their anchorage in the surface area of the body, it is logical to expect that the *amount* of wool and feathers would be proportional not to body weight but to the surface area of the body. Unfortunately there is some uncertainty as to what biological unit of *amount* of hair or feathers one should adopt. Should it be the *number* of hairs or feathers? There are objections to number as unit of covering, because the length and structure of the individual hairs or feathers vary. There are, likewise, objections to *weight* as unit of covering because, especially in feathers, the structural part, such as the quill, is a very substantial part of the feather weight, yet its heat-regulating function is probably slight.

Lacking rational units of "amounts" of hairy or feathery covering, *wool weight*, *feather weight*, and also *feather number* were related[48] to *body weight* and also to *surface area* by the parabola $Y = aX^b$, with results shown in Figs. 17.27 and 17.28a to c.

In *yearling* Shropshire sheep, wool weight is practically proportional to surface area. Both vary with approximately the 0.5 power of body weight. In older animals, however, wool weight does not increase as rapidly as surface area. Unlike wool weight, feather *weight* is almost directly proportional to body weight. Feather *number*, however, increases less rapidly than surface area with increasing body weight. Feather *weight* increases with the first power of body weight, while feather *number* increases approximately with the 0.2 power of body weight.

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[46] *Cf.* Baldwin, B. T., "The physical growth of children from birth to maturity." *Univ. Iowa Studies in Child Welfare*, **I**, No. 1 (1921).

[47] Greulich, W. W., "Handbook of methods for the study of adolescent children." Monographs *Soc. Res. Child. Dev.* No. 2, p. 1, p. 53 (1938). Shuttleworth, F. K., "Sexual maturation and the physical growth of girls age six to nineteen," *Id.*, Vol. 2, No. 5 (1937).

[48] Brody, S., and Campbell, J., Univ. Mo. Agr. Exp. Sta. Res. Bull., 287, 1938.

The physiologic (thermoregulatory) significance of the above results will remain uncertain until a "physiologic unit" of wool or feathers is discovered. The fact that feather *number* and feather *weight* increase at such widely different relative rates suggests that probably neither is a satisfactory index of insulating or thermoregulatory capacity of feathers, and that a mechanical necessity not related to thermoregulation enters the observed relationships. Thus the weight of the supporting quill must, for mechanical reasons, increase more rapidly than that of the insulating vanes.

17.10: Summary. It is shown that to maintain homeostasis the body must change in form during growth, that is, with increasing weight. This chapter is not concerned with the detailed mechanisms of this change, but with the numerical interrelations between visceral organs, functional level and body weight, and linear size and body weight. The form of an animal at any time is the resultant of many factors, one of which is balance between geometric law on one hand and necessity for physiologic stability or homeostatis on the other.

Function is intimately correlated with structure and form. The art of animal judging is based on insight into these correlations; this art is crude because only the grosser aspects of form and structure are available for examination and comparison. The principle that function is an expression of structure is, however, unassailable. Thus a given level of milk production is an expression of certain structural details and organization, for example, structure and size of the mammary gland, cardio-respiratory system, digestive system, endocrine system, and so on. Likewise, the excellence of a work- or race-horse is the expression of the quality and size of its cardio-respiratory system, locomotory system, and so on. Similarly intellectual and emotional, or temperamental, characteristics are expressions of the relative quantity and structure of brain and nervous system, endocrine system, and no doubt of the more vegetative systems, such as cardio-respiratory, digestive, excretory, and so on. To quote Carrel[49], "Structure and function are two aspects of the same thing. Each structural detail possesses its functional expression. . . . The significance of a given structural state is bound to the knowledge of the corresponding physiological state. Structure and function must be considered simultaneously."

The parabola $Y = aX^b$ is the most satisfactory empirical[50] equation for relating part to part or to whole of structure or function in animals of different size. The parabola is one of the three commonly employed equations in the physical sciences and engineering, and it is equally useful in biology. (The other two are the exponential, used for growth (Ch. 16), and the linear, which is included in the parabolic when $b = 1$.) The applicability of this equation to data means only that an increase of 1 per cent in X is associated with an increase of b per cent in Y. This is all it means. Thus, the equation relating basal metabolism, Y, to body weight, X (Ch. 13), by the equation $Y = 70.5X^{0.73}$ merely states that a body weight increase of 1 per cent is associated with a basal metabolism increase of 0.73 per cent; increasing body weight 100 per cent increases basal metabolism 73 per cent; or the ratio of $Y/X^{0.73} = 70.5$. While this equation is empirical, it is extremely useful because of its wide, clear-cut descriptive powers and its manipulative simplicity.

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[49] Carrel, A., "The new cytology," *Science*, **73**, 298 (1931).

[50] *Cf.* Teissier, G., *Ann. Physiol et physico-chim biol.*, **12**, 527 (1936), and *Travaux Station Roscoff*, **9**, 29–239 (1931).

This parabola was employed successfully for relating many visceral organs to body weight. In most cases the value of the exponent, b, is less than unity, near 0.7 or 0.8. This is especially true for the metabolism-activating organs, that is, members of the neuro-endocrine system, and more particularly the brain, including the pituitary.

The weight of blood and heart have the highest value of b; the blood and heart come nearest to varying directly with body weight in mature animals of different species. There are, however, considerable species differences in relative heart weight, depending on relative physical exertion. Athletic species have larger hearts than non-athletic, just as, usually, the more intelligent species have larger brains then the less intelligent. There are, of course, individual exceptions.

This parabola was also employed successfully for relating body weight to linear size in cattle, and the result used for estimating weight from chest girth and nutritive condition from height at withers. In this species, weight varies approximately with the third power of chest girth and with the fourth power of height at withers. Chest girth comes nearest to meeting the theoretical expectation that volume (weight) varies with the cube of linear size; chest girth is thus the best index of body weight. Height at withers is the best reference base for nutritive condition in cattle (and similar grazing animals), because in these animals height at withers, unlike chest girth, is relatively independent of environmental conditions. This is not the case for height growth in man, because most of the height growth is post-natal and also, unlike cattle, the post-natal human curve of growth in height has four apparently distinct segments, each having a different value of b ranging from 1.6 to 2.8.

Wool production increases with approximately the 0.5 power of body weight, as does surface area; that is, increasing body weight by 1 per cent increases wool weight in yearlings by about 0.5 per cent. The increase in wool production is somewhat less at more advanced age. Feather *weight* increase more rapidly than feather *number*, less rapidly than surface area.

Beginning with puberty, linear growth follows the same course, that represented by the equation $Y = A - Be^{-kt}$ as weight growth; but the rate, k, of approach to mature size is different. Preceding puberty, when the rate of weight growth increases exponentially (at a constant *percentage* rate and at *increasing* time rate) the rate of linear growth is at a *constant time rate*. Each of the 21 different kinds of linearly measured complexes in cattle discussed in the text has a different growth constant, k, reflecting the age changes in form and, consequently, function. Growth after puberty, or after the major inflection, follows the same "ground plan" regardless of whether it be weight or linear size; preceding puberty, however, the patterns are different.

Several important "prediction" tables are presented and illustrated by charts.

17.11: Appendix. This appendix includes the tables which could not be included in the text because of overcrowding.

TABLE 17.1. THE RELATION OF ORGAN WEIGHT TO BODY WEIGHT IN APPROXIMATELY MATURE ANIMALS OF DIFFERENT SPECIES

Animals	Live Weight (kg)	Organ Weight									
		Heart (gm)	Liver (gm)	Lung (gm)	Blood (gm)	Stomach and Intestines (gm)	Kidney (gm)	Brain (gm)	Pituitary (gm)	Adrenal (gm)	Thyroid (gm)
Dairy cows	488	1880	6400	3600	21,300	25,200	1160	400	3.2	31	34
Steers	700	2300	5000	3900	25,000		1000	500			
Sheep	52	280	960	710	1,100	2,900	160	106		8	10
Hogs	125	350	1600		4,900	2,200	260	120		6	7.5
Horses	600	4250	6700	5400			1660	670		40	42
Chickens	1.3	7	28	10	50	90	10	4		.19	.19
Dogs	10	85	420	120	700	1,500	70	75		1.3	1.0
Rats	.25	.94	12	1.3	15	20	2.1	2	.015	.048	.038
Guinea pigs	.8	2.3	27	5.0	28		5.6	4.7	.017	.65	.13
Monkeys	4.5	23	110	30	300		21	42		1.0	.55
Humans	60	320	1700		4,300		250	1300		13	24
Elephant	6,650	2,200	6300				1200	5700		44	36
Whales	58,000							4500		1380	
Whales	122,000	631,000			8,000,000						

Animals	Live Weight (lbs)	Organ Weight							
		Heart	Liver	Lung	Blood	Kidney	Brain	Adrenal (oz)	Thyroid (oz)
Dairy cows	1,076	4.1 lbs	14.1 lbs	7.9 lbs	47 lbs	2.6 lbs	14 oz	1.1	1.2
Steers	1,540	5.1 lbs	11 lbs	8.6 lbs	55 lbs	2.2 lbs	18 oz		
Sheep	115	10 oz	2.1 lbs	1.6 lbs	2.4 lbs	5.6 oz	3.6 oz	.28	.35
Hogs	275	12 oz	3.5 lbs		10.8 lbs	9 oz	4 oz	.21	.26
Horses	1,320	9.4 lbs	14.8 lbs	11.9 lbs		3.7 lbs	1.5 lbs	1.4	1.5
Chickens	2.9	.25 oz	1 oz	.35 oz	1.8 oz	.35 oz	.14 oz	.007	.007
Dogs	22	3 oz	15 oz	4.2 oz	1.5 lbs	2.5 lbs	2.6 oz	.046	.035
Monkeys	9.9	.8 oz	3.9 oz	1.1 oz	11 oz	7.4 oz	1.5 oz	.035	.019
Humans	132	11 oz	3.7 oz		9.5 lbs	9 oz	2.9 lbs	.46	.85
Elephant	14,600	4.8 lbs	13.9 lbs			2.6 lbs	12.6 lbs	1.55	1.26

TABLE 17.2. PREDICTION TABLE AND STATISTICAL CONSTANTS FOR FITTED EQUATIONS Organ Wt. = a (Body Wt.)^b For Mature Dairy Cattle of Different Live Weights

Body Weight	Liver	Blood	Heart	Lungs	Intestines	Stomach	Brain
(lbs)	Organ Weights, Pound System						
	(lbs)	(lbs)	(lbs)	(lbs)	(lbs)	(lbs)	(ozs)
800	10.5	34.4	3.78	6.22	18.5	35.7	14.9
850	10.9	35.7	3.91	6.42	19.0	36.4	15.0
900	11.4	37.0	4.04	6.62	19.5	37.2	15.1
950	11.8	38.2	4.16	6.81	20.0	37.8	15.2
1000	12.2	39.4	4.28	6.99	20.4	38.5	15.3
1050	12.6	40.6	4.40	7.18	20.9	39.1	15.4
1100	13.0	41.8	4.52	7.35	21.3	39.8	15.5
1150	13.4	42.9	4.63	7.52	21.7	40.4	15.6
1200	13.7	44.1	4.74	7.70	22.2	41.0	15.6
1250	14.1	45.2	4.85	7.86	22.6	41.5	15.7
1300	14.5	46.2	4.96	8.02	23.0	42.1	15.8
1350	14.8	47.3	5.07	8.18	23.4	42.6	15.8
1400	15.2	48.4	5.17	8.34	23.7	43.1	15.9
1450	15.6	49.4	5.27	8.50	24.1	43.6	16.0
1500	15.9	50.5	5.37	8.65	24.5	44.1	16.0
1550	16.3	51.5	5.47	8.80	24.8	44.6	16.1
1600	16.6	52.5	5.57	8.95	25.2	45.1	16.2
(kg)	Organ Weights, Kilogram System						
	(kg)	(kg)	(kg)	(kg)	(kg)	(kg)	(gm)
350	4.66	15.3	1.68	2.77	8.26	16.0	420
375	4.87	15.9	1.75	2.87	8.51	16.4	424
400	5.09	16.6	1.81	2.97	8.76	16.7	427
425	5.29	17.2	1.87	3.07	9.00	17.1	430
450	5.50	17.8	1.94	3.16	9.23	17.4	433
475	5.70	18.4	1.99	3.25	9.46	17.7	436
500	5.90	19.0	2.05	3.34	9.68	18.0	438
525	6.09	19.5	2.11	3.42	9.89	18.4	441
550	6.28	20.1	2.16	3.51	10.1	18.6	443
575	6.47	20.7	2.22	3.59	10.3	18.9	445
600	6.65	21.2	2.27	3.67	10.5	19.2	448
625	6.83	21.7	2.32	3.75	10.7	19.5	450
650	7.01	22.3	2.38	3.83	10.9	19.7	452
675	7.19	22.8	2.43	3.91	11.1	20.0	454
700	7.36	23.3	2.48	3.98	11.2	20.2	456
725	7.53	23.8	2.52	4.06	11.4	20.5	458
(1) b	.66	.61	.56	.52	.45	.34	.12
(2) S_b	.08	.10	.07	.10	.06	.07	.06
(3) ρ	.50	.39	.50	.34	.44	.33	.13*
(4) $+S_R$, %	13.8	17.7	11.6	18.0	10.8	8.6	10.8
(5) $-S_R$, %	12.1	15.0	10.4	15.3	9.7	7.9	9.7
(6) a	.127 lb .097 kg	.58 lb .43 kg	.018 lb .064 kg	.187 lb .128 kg	.94 lb .61 kg	3.76 lb 2.22 kg	6.82 oz 193 gm

(1) The constant b represents approximately (exactly for exceedingly small changes) the percentage change in organ weight corresponding to a 1% change in body weight. Thus, when the body weight increases from 850 to 950 pounds, which is a change of 11.76%, the intestines increase from 19.0 to 20.0 pounds, which is a change of 5.26%.

$$\text{Therefore, } b = \frac{5.26}{11.76} = .45.$$

(2) The constant S_b is the standard error of the slope b. For similar sets of data (204 cows of various breeds the values of b could be expected two times out of three to differ from our values of b by not more than $\pm S_b$.

(3) The constant, ρ, the coefficient of correlation of the logarithms of the variables, indicates the degree of relationship between variables.

(4) & (5) The constants $+S_R$ and $-S_R$, called the standard error of estimate, indicate the percentage range about the fitted line that includes ⅔ of the data. For example, the weight of intestines of similar 950 pound cows would not be expected more than one time in three to exceed 20 pounds by more than .108 × 20 = 2.16 pounds, or fall below 20 pounds by more than .097 × 20 = 1.94 pounds.

(6) The constant a is empirical, and unlike the other statistical constants depends on the units employed.

* Not significant.

TABLE 17.3. ORGAN WEIGHT AS PERCENTAGE OF BODY WEIGHT, MATURE ANIMALS OF DIFFERENT SPECIES, COMPUTED FROM THE FITTED EQUATION $Y = aX^b$

Body Wt. (gm)	Body Wt. (oz)	Brain (%)	Thyroid (%)	Adrenal (%)	Pituitary (%)	Heart (%)	Kidney (%)	Lung (%)	Liver (%)	Blood (%)	S & I. (%)
10	.35	4.02	.0183	.0693	.0073	.634	1.49	1.200	6.14	5.37	9.80
20	.71	3.26	.0174	.0602	.0062	.626	1.34	1.193	5.60	5.32	9.40
30	1.06	2.88	.0168	.0555	.0057	.622	1.26	1.187	5.31	5.30	9.18
40	1.41	2.64	.0165	.0524	.0053	.620	1.20	1.182	5.11	5.28	9.03
50	1.76	2.47	.0162	.0501	.0050	.617	1.16	1.178	4.96	5.27	8.91
60	2.12	2.34	.0160	.0482	.0048	.616	1.13	1.176	4.84	5.25	8.81
70	2.47	2.23	.0158	.0468	.0046	.614	1.10	1.173	4.74	5.24	8.73
80	2.82	2.14	.0156	.0455	.0045	.613	1.08	1.171	4.66	5.24	8.66
90	3.18	2.07	.0155	.0444	.0044	.611	1.06	1.169	4.59	5.23	8.60
100	3.53	2.00	.0154	.0435	.0042	.610	1.04	1.167	4.52	5.22	8.55
200	7.06	1.62	.0146	.0378	.0036	.604	.938	1.156	4.12	5.18	8.20
300	10.6	1.44	.0141	.0349	.0033	.599	.881	1.150	3.91	5.15	8.01
400	14.1	1.32	.0138	.0329	.0031	.597	.843	1.146	3.76	5.13	7.88
(gm)	(lbs)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
500	1.10	1.23	.0136	.0314	.0029	.595	.814	1.142	3.65	5.12	7.77
600	1.32	1.16	.0134	.0303	.0028	.593	.792	1.139	3.56	5.10	7.69
700	1.54	1.11	.0133	.0294	.0027	.591	.773	1.137	3.49	5.09	7.62
800	1.76	1.07	.0131	.0286	.0026	.590	.757	1.134	3.43	5.08	7.56
900	1.98	1.03	.0130	.0279	.0025	.589	.744	1.132	3.38	5.08	7.50
(kgs)	(lbs)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
1	2.20	.996	.0129	.0273	.0025	.588	.732	1.131	3.33	5.07	7.46
2	4.41	.808	.0122	.0234	.0021	.581	.658	1.120	3.04	5.02	7.16
3	6.61	.714	.0119	.0219	.0019	.577	.618	1.114	2.88	5.00	6.99
4	8.82	.654	.0116	.0207	.0018	.575	.591	1.110	2.77	4.98	6.87
5	11.0	.612	.0114	.0197	.0017	.572	.571	1.106	2.69	4.97	6.78
6	13.2	.579	.0113	.0191	.0016	.571	.555	1.104	2.62	4.96	6.71
7	15.4	.552	.0111	.0185	.0015	.569	.542	1.101	2.57	4.95	6.64
8	17.6	.530	.0110	.0179	.0014	.568	.531	1.099	2.53	4.94	6.59
9	19.8	.512	.0109	.0175	.0014	.567	.521	1.097	2.49	4.93	6.54
10	22.0	.496	.0108	.0171	.0014	.566	.513	1.096	2.45	4.93	6.51
20	44.1	.402	.0102	.0149	.0012	.560	.461	1.085	2.24	4.88	6.24
30	66.1	.355	.0099	.0137	.0011	.556	.433	1.079	2.12	4.86	6.09
40	88.2	.325	.0097	.0129	.0010	.553	.414	1.075	2.04	4.84	5.99
50	110	.304	.0095	.0124	.0009	.551	.400	1.072	1.98	4.83	5.91
60	132	.288	.0094	.0119	.0009	.550	.389	1.069	1.93	4.82	5.85
70	154	.274	.0093	.0115	.0008	.548	.380	1.066	1.89	4.81	5.80
80	176	.264	.0092	.0112	.0008	.547	.372	1.065	1.86	4.80	5.75
90	198	.254	.0091	.0110	.0008	.546	.365	1.063	1.83	4.79	5.71
100	220	.246	.0090	.0107	.0008	.545	.359	1.062	1.81	4.78	5.68
200	441	.200	.0086	.0093	.0006	.539	.323	1.056	1.65	4.74	5.44
300	661	.177	.0084	.0086	.0006	.536	.304	1.046	1.56	4.72	5.32
400	882	.162	.0082	.0082	.0005	.533	.290	1.042	1.50	4.70	5.23
500	1102	.151	.0080	.0078	.0005	.531	.280	1.038	1.46	4.69	5.16
600	1323	.141	.0079	.0075	.0005	.529	.273	1.036	1.42	4.68	5.10
700	1543	.136	.0078	.0072	.0005	.528	.266	1.033	1.39	4.67	5.06
800	1764	.131	.0077	.0070	.0005	.527	.261	1.032	1.37	4.66	5.02
900	1984	.126	.0076	.0069	.0004	.526	.256	1.030	1.35	4.65	4.98
1000	2205	.122	.0076	.0067	.0004	.525	.252	1.029	1.33	4.65	4.95
2000	4409	.099	.0072	.0058	.0004	.519	.226	1.019	1.21	4.61	4.75
3000	6614	.088	.0070	.0054	.0003	.515	.213	1.013	1.15	4.58	4.64
4000	8818	.080	.0068	.0051	.0003	.513	.203	1.009	1.11	4.57	4.56
5000	11023	.075	.0067	.0049	.0003	.511	.196	1.006	1.07	4.56	4.50
50000	110231	.037	.0056	.0030	.0001	.493	.138	.975	.79	4.43	3.93
100000	220462	.030	.0053	.0026	.0001	.487	.124	.965	.72	4.39	3.77

TABLE 17.4. ORGAN WEIGHTS FOR GIVEN BODY WEIGHTS OF MATURE ANIMALS OF DIFFERENT SPECIES COMPUTED FROM THE EQUATION $Y = aX^b$ FITTED TO THE DATA BY THE METHOD OF LEAST SQUARES

Body Wt. (gm)	Brain Wt. (gm)	Thyroid Wt. (mg)	Adrenal Wt. (mg)	Pituitary Wt. (mg)	Heart Wt. (gm)	Kidney Wt. (gm)	Lung Wt. (gm)	Liver Wt. (gm)	Blood Wt. (gm)	S & I. (gm)
10	.402	1.83	6.93	.734	.0634	.149	.120	.614	.537	.980
20	.652	3.48	12.0	1.24	.125	.268	.239	1.12	1.06	1.88
30	.865	5.06	16.6	1.70	.187	.377	.356	1.59	1.59	2.75
40	1.06	6.60	20.9	2.11	.248	.481	.473	2.04	2.11	3.61
50	1.24	8.10	25.0	2.50	.309	.581	.589	2.48	2.63	4.45
60	1.40	9.59	29.0	2.88	.369	.678	.705	2.90	3.15	5.29
70	1.56	11.1	32.7	3.24	.430	.772	.821	3.32	3.67	6.11
80	1.71	12.5	36.4	3.58	.490	.864	.937	3.73	4.19	6.93
90	1.86	14.0	40.0	3.92	.550	.954	1.05	4.13	4.70	7.74
100	2.00	15.4	43.5	4.25	.610	1.04	1.17	4.52	5.22	8.55
200	3.24	29.2	75.7	7.20	1.21	1.88	2.31	8.25	10.4	16.4
300	4.30	42.4	105	9.81	1.80	2.64	3.45	11.7	15.4	24.0
400	5.26	55.3	132	12.2	2.39	3.37	4.58	15.0	20.5	31.5
500	6.15	68.0	157	14.5	2.97	4.07	5.71	18.3	25.6	38.8
600	6.98	80.5	182	16.6	3.56	4.75	6.83	21.4	30.6	46.1
700	7.77	92.8	206	18.7	4.14	5.41	7.96	24.4	35.7	53.3
800	8.53	105	229	20.7	4.72	6.06	9.08	27.4	40.7	60.4
900	9.26	117	251	22.7	5.30	6.69	10.2	30.4	45.7	67.5
(kg)	(gm)	(gm)	(gm)	(gm)	(gm)	(gm)	(gm)	(gm)	(gm)	(gm)
1	9.96	.129	.273	.0246	5.88	7.32	11.3	33.3	50.7	74.6
2	16.2	.245	.475	.0417	11.6	13.2	22.4	60.8	100	143
3	21.4	.356	.657	.0568	17.3	18.5	33.4	86.4	150	210
4	26.2	.464	.827	.0707	23.0	23.6	44.4	111	199	275
5	30.6	.571	.988	.0838	28.6	28.6	55.3	134	248	339
6	34.7	.675	1.14	.0963	34.3	33.3	66.2	158	298	402
7	38.7	.779	1.29	.108	39.9	38.0	77.1	180	346	465
8	42.4	.881	1.44	.120	45.5	42.5	87.9	202	395	527
9	46.1	.982	1.58	.131	51.0	46.9	98.8	224	444	589
10	49.6	1.08	1.72	.142	56.6	51.3	110	245	493	651
20	80.4	2.05	2.99	.241	112	92.2	217	447	977	1250
30	107	2.99	4.13	.328	167	130	324	636	1460	1830
40	130	3.90	5.20	.413	222	166	430	816	1940	2400
50	152	4.79	6.21	.485	276	200	536	990	2410	2950
60	173	5.67	7.18	.557	330	234	642	1160	2890	3510
70	192	6.53	8.12	.626	384	266	747	1330	3360	4060
80	211	7.39	9.03	.694	438	298	852	1490	3840	4600
90	229	8.24	9.92	.759	492	329	957	1650	4310	5140
100	247	9.08	10.8	.822	545	360	1060	1810	4780	5680
200	400	17.2	18.8	1.39	1080	647	2100	3290	9490	10900
300	531	25.1	25.9	1.90	1610	911	3140	4680	14200	16000
400	648	32.7	32.6	2.36	2130	1160	4170	6010	18800	20900
500	758	40.2	39.0	2.80	2660	1400	5190	7290	23400	25800
600	850	47.6	45.1	3.22	3180	1640	6220	8540	28100	30600
700	958	54.8	51.0	3.62	3700	1870	7240	9760	32700	35400
800	1050	62.0	56.8	4.01	4220	2090	8260	11000	37300	40100
900	1140	69.1	62.3	4.39	4740	2310	9270	12100	41900	44800
1000	1230	76.2	67.8	4.76	5250	2520	10300	13300	46500	49500
2000	1990	145	118	8.07	10400	4540	20400	24300	92200	95000
3000	2640	210	163	11.0	15500	6390	30400	34500	138000	139000
4000	3230	274	205	13.7	20500	8150	40400	44300	183000	182000
5000	3770	337	245	16.2	25600	9850	50300	53700	228000	225000
50000	18800	2830	1540	93.8	246000	69000	488000	396000	2210000	1960000
100000	30400	5360	2680	159	487000	124000	966000	721000	4390000	3770000

Body Wt. (lbs)	Brain Wt. (lbs)	Thyroid Wt. (oz)	Adrenal Wt. (oz)	Pituitary Wt. (oz)	Heart Wt. (lbs)	Kidney Wt. (lbs)	Lung Wt. (lbs)	Liver Wt. (lbs)	Blood Wt. (lbs)	S. & I. (lbs)
.1	.00254	.000261	.000816	.0000822	.000618	.00118	.00118	.00502	.00528	.00895
.2	.00412	.000495	.00142	.000139	.00122	.00212	.00234	.00916	.0105	.0172
.3	.00547	.000720	.00196	.000190	.00182	.00298	.00349	.0130	.0156	.0252
.4	.00668	.000940	.00247	.000236	.00242	.00381	.00463	.0167	.0207	.0330
.5	.00780	.00116	.00295	.000280	.00301	.00460	.00577	.0203	.0258	.0407
.6	.00886	.00137	.00341	.000322	.00360	.00537	.00690	.0238	.0309	.0482
.7	.00987	.00158	.00386	.000362	.00419	.00611	.00804	.0272	.0360	.0559
.8	.0108	.00178	.00429	.000401	.00478	.00684	.00917	.0305	.0411	.0634
.9	.0118	.00199	.00471	.000438	.00537	.00756	.0103	.0338	.0462	.0708
1	.0126	.00219	.00512	.000475	.00595	.00827	.0114	.0370	.0512	.0781
2	.0205	.00416	.00891	.000806	.0118	.0149	.0226	.0674	.102	.150
3	.0272	.00605	.0123	.00110	.0176	.0209	.0338	.0959	.152	.220

TABLE 17.4.—*Continued*

Body Wt. (lbs)	Brain Wt. (lbs)	Thyroid Wt. (oz)	Adrenal Wt. (oz)	Pituitary Wt. (oz)	Heart Wt. (lbs)	Kidney Wt. (lbs)	Lung Wt. (lbs)	Liver Wt. (lbs)	Blood Wt. (lbs)	S. & I. (lbs)
4	.0333	.00789	.0155	.00137	.0233	.0267	.0448	.123	.201	.288
5	.0388	.00970	.0185	.00162	.0290	.0323	.0559	.149	.251	.355
6	.0441	.0115	.0214	.00186	.0347	.0376	.0669	.175	.300	.422
7	.0491	.0132	.0242	.00209	.0404	.0429	.0778	.200	.350	.488
8	.0539	.0150	.0269	.00232	.0461	.0480	.0888	.224	.399	.553
9	.0585	.0167	.0296	.00254	.0517	.0530	.0997	.248	.448	.618
10	.0630	.0184	.0322	.00275	.0574	.0580	.111	.272	.497	.682
20	.102	.0349	.0560	.00466	.114	.104	.219	.497	.985	1.31
30	.136	.0508	.0773	.00634	.169	.147	.327	.706	1.47	1.92
40	.165	.0662	.0973	.00790	.224	.187	.434	.906	1.95	2.52
50	.193	.0814	.116	.00936	.280	.226	.541	1.10	2.43	3.10
60	.220	.0964	.134	.0108	.335	.264	.647	1.29	2.91	3.68
70	.244	.111	.152	.0121	.389	.301	.754	1.47	3.39	4.26
80	.268	.126	.169	.0134	.444	.337	.860	1.65	3.87	4.83
90	.291	.140	.186	.0146	.499	.372	.965	1.83	4.35	5.39
100	.314	.154	.202	.0159	.553	.407	1.07	2.00	4.82	5.96
200	.508	.293	.351	.0269	1.09	.731	2.12	3.66	9.56	11.4
300	.674	.426	.486	.0367	1.63	1.03	3.16	5.20	14.3	16.8
400	.824	.556	.611	.0457	2.16	1.31	4.20	6.67	19.0	22.0
500	.962	.683	.730	.0541	2.70	1.59	5.24	8.09	23.6	27.1
600	1.09	.809	.844	.0622	3.22	1.85	6.27	9.48	28.3	32.2
700	1.22	.933	.955	.0699	3.75	2.11	7.30	10.8	32.9	37.2
800	1.34	1.06	1.06	.0774	4.28	2.36	8.32	12.2	37.6	42.2
900	1.45	1.18	1.17	.0847	4.81	2.61	9.35	13.5	42.2	47.1
1000	1.56	1.30	1.27	.0918	5.33	2.85	10.4	14.8	46.8	52.0

TABLE 17.5. KEY TO SOME OF THE SOURCES OF DATA USED IN PREPARING THE CHARTS FOR THIS CHAPTER

Number of Averages* or Individuals*

Animal	Ref. No.§	Brain	Thyroid	Adrenal	Pituitary	Heart	Kidney	Lung	Liver	Blood
Mouse, white	1								7M	1M
Mouse	2									
Rat, albino	3		14A*, 63G*♀; 25A, 91G♂	14A, 113G♀; 24A, 145G♂	15A, 78G♀; 14A, 113G♂	36A, 135G♂ & ♀	36A, 130G♂ & ♀	32A, 78G♂ & ♀	36A, 130G♂ & ♀	
Rat, albino	4					134G♂				
Rat, albino	5		M, A5♂, A12♀			M, A5♂, A20♀				
Rat, albino	6	M, A50♀, A50♂		M, A50♀, A50♂	M, A50♀, A50♂		M, A50♀, A50♂	M, A50♀, A50♂	M, A50♀, A50♂	
Rat, albino	6	M, A51♀, A50♂		M, A51♀, A50♂	M, A51♀, A50♂		M, A51♀, A50♂	M, A51♀, A50♂	M, A51♀, A50♂	
Rat, albino	7					M, A98♀, A70♂				
Rat, albino	8	26A, 250G♂; 23A, 213G♀								
Rat, albino	8	M, A7♂, A6♀			M, A10♀					
Rat, albino	9									20A, 154G♂ & ♀
Rat, albino	10									
Mammals, various	11	71A, 135M♂ & ♀				39G				
Frog	12					11G				
Fish	12					9G				
Turtle	12			M, A44♀, A6♂		A77♂, A117♀				
Guinea pig	13			M, A175♀, A458♂	M, A175♀, A457♂		M, A175♀, A457♂	M, A74♀, A325♂	M, A175♀, A457♂	M, A155♀, A238♂
Guinea pig	14		M, A74♀, A300♂			A20	A20	A20	A20	
Chicken	15					7A, 70G♀, 7A, 70G♂	A10♀, A10♂			
Chicken, W.L.	16					4A, 20G♀, 9A, 45G♂	M, A5♀, A5♂	4A, 20G♀, 9A, 45G♂	4A, 20G♀, 9A, 45G♂	4A, 20G♀, 9A, 45G♂
Chicken, W.P.R.	17			21A, 209G♂ & ♀						
Chicken, Leghorn	18	21A, 215G♂ & ♀	21A, 215G♂ & ♀			9A	7A	8A	9A	
Chicken, embryo	19	8A				7A	5A	6A	7A	
Pigeon embryo	19	6A				12A, 120G	12A, 120G		12A, 120G	
Pigeon immature	20			262♂ & ♀	231G♂ & ♀					
Cat, fetal	21		242G♂ & ♀	M, A52♂, A52♀	M, A52♂, A52♀					
Cat, mature	22		M, A52♂, A52♀				M, A11♀, A9♂			
Cat, growing	23						31G♂, 22G♀			
Cat, growing	24									
Cat, growing	13			M, A65♀, A47♂		G, 95♀, 74♂				
Dog, growing	13			M, A12♀, A15♂		G, 22♀, 23♂				

TABLE 17.5 (*Continued*)

Dog, growing	25	7A, 47G				34G♂ & ♀	34G♂ & ♀	34G♂ & ♀	34G♂ & ♀	11G♂ & ♀
Dog, growing	26			33A, 292G♂; 31A, 282G♀						
Dog, growing	27					84G♂ & ♀				
Dog, growing	28					13G♂ & ♀	M, 1♀, A7♂	13G♂ & ♀		
Monkey	29	13G♂ & ♀				M, A10♂, A10♀	M, A10♂, A10♀	M, A♂10, A10♀	M, A10♂, A10♀	
Turkey	30					M, A4♀, A6♂				
Man	31					A♂	A♂	A♂	A	A♂
Man	32					10A, 60G	A10M	A10M		A10M
Swine	33	A10M				A10M♀	A 9M♀	A9M♀	A9M♀	A9M♀
Swine	34	A9M♀				A25♀	A25M♀			
Cattle, Simmentaler	35					A25♀	A25M♀			
Cattle, Oldenburger	35			A102M♀	A105M♀	A104M♀	A108M♀	A106M♀	A107M♀	A108M♀
Cattle, Jersey	36	A107M♀	A106M♀	A 88M♀	A 93M♀	A 93M♀	A 93M♀	A 98M♀	A 96M♀	A 96M♀
Cattle, Holstein	36	A 98M♀	A 95M♀	A 30M♀	A 31M♀	A 30M♀	A 31M♀	A 30M♀	A 31M♀	A 30M♀
Cattle, Guernsey	36	A 31M♀	A 31M♀	A 19M♀	A 22M♀	A 22M♀	A 22M♀	A 22M♀	A 22M♀	A 22M♀
Cattle, Ayrshire	36	A 22M♀	A 20M♀	A 33M♀	A 33M♀	A 33M♀	A 34M♀	A 35M♀	A 34M♀	A 33M♀
Cattle, Grades	36	A 35M♀	A 33M♀	A 2M♀	A 2M♀	A 2M♀	A 2M♀		A 2M♀	A 2M♀
Cattle, Holstein	37	A 2M♀	A 2M♀			A 7M	A 3M		A 7M	A 7M
Hereford steers	38	A 7M				10G	10G		10G	10G
Hereford steers	39	10G		A2M♀	A2M♀				A2M♀	A2M♀
Hereford	37	A2M♀	A2M♀			204G♀		204G♀	204G♀	204G♀
Cattle, various	40	204G♀								A8, A9
Lambs	41			31G & M		31G & M	36G & M	36G & M	37G & M	
Horses, various	18		29G & M	8		9	8	9	9	
Horses, fetal	18		9	175A, 1066M♂ & ♀		143A, 947M♂ & ♀	116A, 915M♂ & ♀	116A, 762M♂ & ♀	118A, 845M♂ & ♀	
Mammals, various	18	122A, 835M♂ & ♀	129A, 791M♂ & ♀	70A, 193M♂ & ♀		69A, 191M♂ & ♀	50A, 165M♂ & ♀	53A, 169M♂ & ♀	56A, 176M♂ & ♀	
Birds, various	18	69A, 192M♂ & ♀	69A, 204M♂ & ♀							8A, 469M♂ & ♀
Mammals, various	42			27A, 78M♂ & ♀	22A, 30M♂ & ♀	21A, 29M♂ & ♀	21A, 29M♂ & ♀	21A, 29M♂ & ♀	21A, 29M♂ & ♀	
African ungulates	43	27A, 78M♂ & ♀	27A, 78M♂ & ♀			16A, 117M♂ & ♀				
Mammals, various	44							2		
Whale	45	1M				1M		1M	A2M♂	1M
Whale	46				10A, 806M♂ & ♀					
Mammals, various	47									
Mammals, various	48	72A, 129M♂ & ♀				Monthly A	Monthly A	Monthly A	Monthly A	
Man, prenatal	49	Monthly A								
Dog	25	M, A9♂, A9♀								
Birds, various	50	M, A45, 144♂ & ♀								

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*A, represents average; G, growing; M, mature. For example, in reference 22, one average of 52 mature males, and another average of 52 females were employed. In reference 20, twelve averages including a total of 120 growing animals were used.

§ See the list of references to the literature in Table 17.6 (page 649).

TABLE 17.6. REFERENCES FOR TABLE 17.5

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TABLE 17.7. THE MEASUREMENTS, THE NUMBERS BY WHICH THE MEASUREMENTS ARE INDICATED ON THE CHARTS, THE VALUES OF THE MEASUREMENTS AT MATURITY (A), THE MONTHLY PERCENTAGE DECLINE IN THE TIME RATE OF GROWTH ($100k$), THE CONSTANTS B, AND t^* (BASED ON AGE COUNTED FROM CONCEPTION AND ON THE ASSUMPTION THAT THE PERIOD OF PRENATAL GROWTH IN DAIRY CATTLE IS 9.4 MONTHS), THE AGES (FROM BIRTH) WHEN ONE HALF, THREE FOURTHS AND 98 PERCENT OF THE MATURE VALUES ARE REACHED. (FOR CHARTS SEE PAGES 598–600.)

Numbers and names of meaurements	The numerical values of the measurements at maturity (A)				Monthly percentage decline in growth (100k)		Empirical Constant (Conception) (B)		t* (from Conception)		Age (from birth at)					
	Jersey		Holstein								One-half mature value		Three fourths mature value		98 percent mature value	
	(cm.)	(in.)	(cm.)	(in.)	Jersey	Holstein	Jersey	Holstein	Jersey (mos)	Holstein (mos)	Jersey (mos)	Holstein (mos)	Jersey (mos)	Holstein (mos)	Jersey (mos)	Holstein (mos)
1. Height at withers	125.9	49.6	134.7	53.0	9.0	8.5	137	139	.94	.47	− .80	− .78	7.0	7.4	35	37
2. Height at highest point of croup	125.0	49.2	133.0	52.4	11.0	11.0	156	168	2.0	2.1	−1.1	− .97	5.2	5.3	28	28
3. Height at hips points	123.0	48.4	132.0	52.0	12.2	11.0	178	164	3.0	2.0	− .72	−1.1	5.0	5.2	26	28
4. Depth of chest just behind elbow joint	65.3	25.7	69.0	27.2	9.5	8.7	96	92	4.1	3.3	2.1	1.9	9.4	9.8	36	39
5. Width of chest just behind elbow joint	40.0	15.7	44.4	17.5	8.0	6.5	57	50	4.4	1.8	3.7	.45	12.4	13.8	44	53
6. Width of hips (hip joints)	50.0	19.7	55.0	21.7	6.7	5.8	66	66	4.1	3.1	5.1	5.7	15.4	17.6	53	61
7. Width of loin (center)	35.7	14.1	39.0	15.4	6.5	6.0	44	44	3.2	2.0	4.5	4.2	15.2	15.7	54	58
8. Length from poll to point of muzzle	49.3	19.4	54.6	21.5	11.5	10.2	86	82	4.8	4.0	1.5	1.5	7.5	8.2	29	33
9. Width of forehead	19.2	75.6	21.0	8.3	15.0	11.0	33	25	3.6	1.6	−1.2	−1.5	3.5	4.8	20	28
10. Circumference of muzzle at opening of mouth	41.0	16.1	45.2	17.8	10.0	10.2	54	45	2.8	0	.27	−2.6	7.2	4.2	33	29
11. Length from horns to base of withers	54.5	21.5	57.5	22.6	10.0	11.0	96	88	5.1	4.3	2.0	1.8	8.3	8.7	31	34
12. From highest point of withers to a line between hips	86.0	33.9	98.0	38.6	9.5	6.8	130	112	4.3	2.0	2.2	2.8	9.5	13.0	36	50
13. From a line between hips to tail																
14. From point of shoulders to point of hips	109.0	42.9	119.0	46.9	11.5	8.7	191	153	4.9	2.9	1.5	1.5	7.5	9.4	30	39
15. From point of shoulders to ischium	155.0	61.0	164.0	64.6	8.8	9.2	205	226	3.2	3.5	1.7	1.6	9.5	9.1	38	37
16. From point of hips to ischium	46.0	18.1	47.0	18.5	9.1	9.1	62	61	3.3	2.9	1.5	4.4	9.1	8.7	37	36
17. From point of hips directly forward to last rib	35.0	13.8	35.0	13.8	7.6	8.7	44	49	3.0	3.8	2.7	6.6	11.9	10.4	45	39
18. Heart girth	170.0	66.9	185.0	72.8	8.3	7.4	220	215	3.1	2.0	2.1	4.1	10.4	11.4	41	46
19. Girth of paunch just behind last rib	200.0	78.7	216.0	85.0	8.6	7.9	268	260	7.1	2.3	5.8	1.7	13.8	10.5	43	43
20. Smallest circumference of shin bone of fore leg	15.5	6.1	17.8	7.0	11.0	8.8	21	18	2.8	1.3	− .34	− .25	2.4	7.6	29	36
21. Smallest circumference of shin bone of hind leg	17.2	6.8	19.9	7.8	11.0	10.0	24	24	3.0	1.9	− .10	− .60	6.2	6.3	29	32
11. + 12 + 13 (Horns to tail)	173 cm	68.1	185 cm	72.8	12.6	10.5	376	311	6.2	4.9	2.3	2.1	8.4	8.8	28	33
22. Weight	420 kgs	926 lbs	550 kgs	1215 lbs	5.4	4.2	680	805	8.9	8.3	13	14	26	60	84	72

TABLE 17.8. DATA OF SKELETAL GROWTH IN JERSEY CATTLE

	1		2		3		4		5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Age	Height at withers		Height at highest point of croup		Height at hip points		Depth of chest just behind elbow joint		Width of chest just behind elbow joint	Width of hips	Width of loins	Length from poll to point of muzzle	Width of forehead	Circumference of muzzle at opening of mouth	Length from base of horns to withers	From highest point of withers to a line between the hips	From a line between hips to the tail	From point of shoulders to point of hips	From point of shoulders to ischium	From point of hips to ischium	From point of hips directly forward to last rib	Heart girth just behind elbow joint	Girth of paunch at end of last rib	Smallest circumference of shin bone	
																								Fore leg	Hind leg
(mos.)	No. animals	(cm.)	No. animals	(cm.)	No. animals	(cm.)	No.* animals	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)
Birth	10	66.8	7	69.5	5	69.4	5	26.5	13.5	14.2	11.2	22	11.4	21.4	20.4	34.0	14.6	48.6	64.6	20.0	12.2	68.2	71.6	8.5	9.6
1	14	71.1	8	75.4	6	75.0	6	29.6	15.7	16.3	13.9	22	12.8	22.5	23.8	38.5	15.8	53.6	72.7	21.6	14.3	75.2	86.1	8.9	9.5
2	17	75.9	9	79.8	11	78.3	7	32.6	17.2	18.2	14.1	26	13.2	24.1	26.6	43.1	15.7	58.6	79.7	23.6	16.0	82.3	97.9	9.5	10.2
3	18	80.4	9	84.9	11	82.9	7	35.9	19.2	20.8	15.9	28	13.7	25.8	29.0	46.6	19.0	63.2	83.2	25.6	18.4	91.5	112.0	9.7	10.7
4	20	84.9	9	90.0	11	88.7	7	38.6	20.6	23.1	17.6	30.1	14.6	26.7	31.6	51.0	20.0	67.7	90.8	27.7	19.6	98.6	119.5	10.5	11.4
5	22	89.6	11	94.1	11	92.5	7	41.9	23.9	25.2	18.9	32.0	14.9	30.4	33.0	55.6	22.1	72.6	99.1	29.4	21.9	106.9	133.6	11.1	12.4
6	24	93.6	15	97.4	14	96.1	11	43.3	24.2	26.7	19.9	35.2	15.6	29.2	37.1	58.3	24.0	78.5	106.8	30.7	21.5	110.8	132.7	11.4	12.8
7	29	96.8	23	98.8	21	99.5	17	44.3	24.9	29.5	20.6	35.6	15.7	30.4	38.3	59.8	28.5	81.1	109.8	31.9	23.2	115.1	140.7	11.7	13.2
8	35	98.5	25	101.8	22	101.4	19	46.4	25.4	29.6	22.3	37.0	15.8	31.3	40.2	61.0	28.9	81.4	111.8	32.8	23.5	118.5	142.7	12.1	13.5
9	34	100.8	29	104.2	24	103.5	21	47.9	27.9	31.0	22.2	38.9	16.6	32.2	42.3	62.1	30.7	84.6	115.6	34.0	24.6	122.5	147.6	12.4	14.0
10	37	102.9	30	106.4	27	105.9	22	49.4	28.0	32.2	22.6	40.0	17.2	32.9	42.9	65.2	32.2	87.7	120.5	35.1	25.2	125.9	149.5	12.8	14.6
11	39	104.9	32	108.6	28	107.8	24	50.5	29.7	33.5	23.2	41.9	17.9	33.4	45.5	65.9	34.0	90.4	123.7	36.2	26.0	129.9	155.3	13.2	15.0
12	41	106.5	32	110.2	28	108.9	24	51.3	29.8	34.2	23.9	42.2	17.6	34.1	46.8	66.8	34.0	91.9	126.1	36.8	26.1	132.1	155.4	13.4	15.2
13	41	108.3	33	111.1	26	109.9	24	51.7	29.9	35.2	24.7	42.6	17.9	34.5	47.1	68.6	34.4	92.4	127.1	37.7	27.0	135.2	156.8	13.7	15.4
14	40	109.7	30	112.3	27	111.9	23	53.4	30.3	35.9	25.4	43.6	17.9	35.1	47.2	69.1	35.0	93.7	129.1	38.1	26.7	137.2	160.1	14.0	15.6
15	42	111.0	32	113.3	27	113.1	24	54.5	31.7	36.5	25.6	43.6	18.4	35.3	48.5	70.3	35.5	95.1	131.6	38.3	27.4	140.2	163.2	14.1	15.6
16	40	111.8	35	114.7	28	113.9	24	55.6	32.2	37.1	26.6	45.0	18.3	35.8	49.2	70.9	36.0	96.5	133.5	38.9	27.6	141.5	165.3	14.1	15.8
17	36	113.2	33	115.4	28	114.7	24	55.8	32.8	38.3	26.7	45.7	18.5	36.0	49.1	72.9	36.8	98.2	135.4	39.3	28.5	145.9	168.6	14.4	16.0
18	41	113.9	34	115.5	29	115.3	26	56.7	33.6	38.7	27.1	45.7	18.7	36.6	49.3	73.9	36.7	99.3	136.9	40.2	29.0	145.5	170.4	14.5	16.3
19	43	115.3	37	116.7	28	115.9	26	57.6	33.2	39.2	27.7	46.4	18.4	36.9	49.6	73.8	36.9	100.3	138.0	40.5	28.9	147.0	170.6	14.7	16.4
20	39	116.1	40	118.3	30	116.8	28	58.5	33.8	40.1	28.1	46.5	18.9	36.9	51.4	75.9	37.0	101.4	139.7	41.5	29.5	149.8	175.1	14.7	16.4
21	40	116.8	43	119.3	32	117.7	30	59.3	34.0	40.8	28.6	46.8	18.6	37.5	50.9	76.6	36.6	102.7	140.5	42.0	29.6	151.1	175.9	14.8	16.3
22	41	117.4	42	115.1	32	118.2	29	59.4	34.4	41.2	28.6	47.5	18.9	38.2	51.9	76.7	36.8	103.6	143.2	42.5	29.8	153.0	177.5	14.9	16.4
23	41	118.7	42	120.1	34	118.9	30	60.5	34.6	42.2	29.6	47.0	18.6	38.2	51.6	77.9	36.5	104.3	144.3	43.2	29.8	154.9	179.7	15.0	16.5
24	40	119.3	40	121.1	33	119.5	31	61.2	35.3	43.1	30.0	47.4	18.7	38.5	52.1	79.8	36.0	105.1	145.7	43.5	29.8	157.4	183.7	15.0	16.8
25	36	119.8	36	121.8	30	120.4	28	61.9	35.5	43.8	30.9	47.4	18.4	39.0	50.8	81.1	36.2	106.0	146.3	44.0	30.9	158.2	186.1	15.1	16.6
26	35	119.9	33	122.1	28	120.8	26	62.0	36.0	44.2	31.2	47.6	18.6	39.1	50.2	82.3	35.0	105.4	145.7	44.0	30.9	158.5	185.0	15.2	16.8
27	37	120.5	34	122.7	28	121.2	25	62.8	37.4	44.9	31.5	47.5	18.8	39.4	49.9	82.3	34.9	106.9	147.7	44.3	31.5	160.2	188.6	15.2	16.8
28	23	120.4	29	123.4	23	121.2	22	63.0	37.1	45.6	32.4	46.5	18.5	39.6	48.5	84.6	32.0	107.7	148.3	44.6	32.0	161.3	190.1	15.1	16.8
29	24	121.0	27	123.8	22	121.5	21	64.1	37.4	45.9	32.7	46.9	18.8	39.9	47.9	85.7	32.9	107.6	148.1	45.0	31.3	162.6	194.6	15.2	16.8
30	31	121.7	26	124.1	21	121.9	20	63.9	37.1	46.2	32.7	47.0	19.0	39.5	49.2	85.2	32.3	108.0	148.2	45.1	32.8	162.5	194.4	15.1	16.7
31	20	122.1	26	124.9	21	122.6	21	63.9	39.3	46.7	33.3	46.8	18.7	39.8	49.5	86.3	32.5	107.5	148.9	45.7	32.7	164.7	196.6	15.1	16.8
32	21	122.3	24	124.8	20	122.5	20	64.4	38.9	47.0	33.8	47.2	18.6	40.0	50.5	85.6	32.4	109.2	150.4	45.5	33.2	166.1	198.8	15.1	16.6
33	30	122.8	21	124.9	17	122.7	18	64.8	39.3	47.8	33.8	47.0	18.5	40.3	52.5	85.5	33.0	110.5	152.1	45.6	32.6	166.7	198.7	15.1	16.6
34	20	122.6	23	125.0	19	122.8	18	64.8	39.2	47.4	33.9	47.1	18.7	39.9	51.6	86.1	33.0	109.4	150.4	46.3	32.9	165.8	194.9	15.1	16.7
35	19	122.8	23	124.9	19	122.9	19	65.1	39.2	47.8	33.9	47.1	18.4	40.2	51.5	86.6	32.7	108.8	150.8	46.0	33.0	166.2	196.4	15.1	16.7
36	31	123.3	22	125.4	18	123.4	19	65.0	41.1	47.6	33.7	47.6	18.6	40.4	52.4	86.5	32.5	108.6	151.0	46.2	33.6	165.5	192.9	15.3	16.8

TABLE 17.9. DATA OF SKELETAL GROWTH IN HOLSTEIN CATTLE

	1		2		3		4		5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Age	Height at withers		Height at highest point of croup		Height at hip points		Depth of chest just behind elbow joint		Width of chest just behind elbow joint	Width of hips	Width of loins	Length from poll to point of muzzle	Width of forehead	Circumference of muzzle at opening of mouth	Length from base of horns to withers	From highest point of withers to a line between the hips	From a line between hips to the tail	From point of shoulders to point of hips	From point of shoulders to ischium	From point of hips to ischium	From point of hips directly forward to last rib	Heart girth just behind elbow joint	Girth of paunch at end of last rib	Smallest circumference of shin bone	
																								Fore leg	Hind leg
(mos)	No. animals	(cm.)	No. animals	(cm.)	No. animals	(cm.)	No. animals	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)	(cm.)
Birth	11	70.4	6	74.1	6	73.5	6	28.4	16.8	16.2	12.9	23.2	11.8	21.5	22.0	38.5	15.3	50.8	60.0	21.5	13.2	76.2	77.0	10.1	10.7
1	20	76.9	8	80.6	13	79.3	8	32.2	18.4	18.3	14.9	25.9	13.1	25.4	26.3	43.0	17.1	55.4	76.0	24.1	14.8	84.6	90.4	10.5	11.2
2	23	81.8	7	85.1	14	85.3	7	35.0	21.0	21.0	16.7	29.7	13.9	27.1	30.9	47.9	18.2	62.3	85.5	25.9	17.0	92.9	111.6	11.0	12.0
3	25	86.6	7	89.8	14	89.8	7	38.1	23.7	22.9	17.9	31.0	14.5	28.3	30.6	51.3	19.6	66.6	90.4	27.0	18.4	100.7	118.0	11.4	12.5
4	23	92.0	8	95.8	15	94.6	8	41.7	24.1	25.8	20.0	32.7	15.5	30.1	33.0	55.9	21.5	71.9	99.5	29.1	20.4	108.4	132.0	12.4	13.5
5	29	96.3	8	100.5	15	99.8	8	44.6	26.5	29.1	20.9	34.0	15.9	31.5	35.9	58.3	22.9	76.4	106.0	31.1	21.3	114.0	136.6	13.0	14.4
6	36	100.1	14	104.6	20	103.9	14	46.9	27.7	29.8	23.4	37.4	16.4	32.8	40.1	61.9	26.9	83.3	112.9	33.1	22.6	120.8	144.2	13.2	14.7
7	37	102.3	19	106.3	25	105.4	20	47.8	28.3	30.5	23.1	39.0	16.8	33.7	42.2	62.9	29.2	85.3	116.2	34.0	23.7	124.1	147.4	13.8	15.5
8	39	104.6	23	108.3	25	107.8	22	49.2	28.9	32.1	24.0	40.2	16.9	34.9	44.4	65.4	30.8	88.3	119.6	35.0	24.9	127.8	153.3	13.9	15.7
9	41	106.9	22	111.5	27	110.4	23	50.9	30.0	33.6	24.8	41.7	17.5	35.4	44.2	67.1	31.2	91.3	124.3	35.5	25.3	132.1	156.2	14.2	15.9
10	41	109.9	22	114.1	23	112.4	22	52.7	31.5	34.6	25.3	42.5	17.6	36.2	45.8	68.5	31.9	91.8	126.1	36.3	26.2	135.1	159.2	14.5	16.2
11	44	110.8	24	115.1	26	113.8	25	53.2	31.3	35.6	26.3	43.3	17.6	36.9	46.1	69.8	31.9	94.7	128.8	37.0	27.0	138.0	161.5	14.6	16.6
12	47	112.6	24	116.8	27	115.2	25	54.5	32.6	36.3	26.7	44.3	18.1	37.6	46.2	71.1	32.8	95.3	130.0	37.5	27.3	140.6	164.7	15.0	17.0
13	48	114.4	24	118.9	27	117.4	24	55.7	32.7	37.2	27.0	45.7	18.6	38.3	48.7	72.3	34.2	98.3	133.7	38.8	28.0	143.7	166.9	15.2	17.4
14	46	116.0	26	119.7	28	118.7	26	55.9	33.9	38.3	28.2	46.2	19.1	39.0	49.0	73.8	34.3	99.9	136.1	39.5	28.4	145.2	169.5	15.3	17.4
15	46	117.3	27	120.9	28	119.7	27	57.9	34.6	39.3	28.4	47.3	19.1	39.6	49.4	75.1	34.9	100.4	137.8	40.3	28.6	148.4	172.4	15.1	17.7
16	47	118.9	28	122.7	30	121.1	28	58.7	34.7	39.9	28.6	49.1	19.7	40.2	50.6	76.1	36.5	102.2	141.3	40.8	29.2	150.7	172.9	15.9	18.0
17	47	119.9	29	123.7	31	122.1	29	59.3	35.8	40.8	29.4	49.1	19.6	40.7	52.4	77.0	36.9	103.5	142.8	41.1	29.1	153.6	177.7	16.2	18.4
18	47	120.9	27	124.2	29	122.9	27	60.6	36.2	41.5	29.6	49.3	20.1	41.1	53.2	76.6	37.5	103.9	144.2	41.6	29.7	155.6	177.9	16.3	18.5
19	49	121.8	30	125.4	31	123.9	29	60.9	36.9	42.2	29.9	50.0	20.0	41.4	52.9	78.4	38.4	105.3	145.2	42.1	29.9	157.4	181.7	16.6	18.7
20	49	123.3	30	126.8	30	125.2	29	62.0	37.2	43.1	30.7	50.6	20.0	42.0	53.9	80.3	38.3	106.0	146.7	42.7	30.4	160.1	185.6	16.7	19.0
21	50	124.1	28	126.8	30	125.4	28	62.1	37.9	43.5	30.8	51.3	20.3	42.2	54.2	80.2	39.0	108.2	149.4	43.3	30.5	161.3	186.5	16.8	19.1
22	49	125.1	27	127.8	30	126.4	27	62.9	37.5	43.4	31.2	51.3	20.2	42.3	53.0	82.7	38.6	108.7	151.0	43.6	30.3	162.2	189.2	16.9	19.1
23	46	125.7	26	129.6	29	127.9	26	64.0	39.3	45.3	32.0	52.5	20.5	43.2	54.7	83.5	38.9	109.0	151.6	44.2	30.9	166.1	193.4	17.2	19.5
24	43	126.7	25	129.5	28	128.1	25	64.2	39.1	45.8	32.1	52.0	20.1	43.1	53.8	84.6	38.0	111.8	152.6	44.1	31.0	166.3	195.6	17.1	19.4
25	38	127.4	22	130.1	18	128.7	22	64.9	36.8	46.8	32.8	51.8	20.0	43.0	55.8	85.4	36.9	111.9	153.6	44.5	32.1	167.4	197.1	17.2	19.4
26	40	127.6	23	130.7	19	128.7	23	65.8	39.9	47.6	33.6	52.5	20.4	43.4	56.7	86.9	38.0	114.7	156.9	45.2	31.9	170.3	201.0	17.2	19.6
27	38	128.3	23	130.8	18	128.7	23	65.8	40.3	47.6	33.7	52.6	20.3	44.3	55.3	86.6	37.2	113.1	156.1	45.1	32.5	170.7	201.0	17.4	19.6
28	35	128.9	22	131.9	19	129.3	22	66.3	41.5	48.1	34.2	52.6	20.3	43.9	53.8	88.9	36.8	114.4	157.3	45.3	32.1	171.2	201.7	17.4	19.6
29	32	129.3	18	131.9	18	129.9	19	66.1	40.6	48.6	34.3	52.0	19.9	44.4	56.0	89.2	36.7	115.1	157.7	45.7	32.4	172.8	203.0	17.3	19.6
30	34	130.4	19	133.0	19	130.7	19	67.5	41.6	51.1	35.4	52.0	19.8	44.3	55.1	90.5	35.0	114.8	158.1	46.4	33.3	174.9	206.4	17.5	19.6
31	21	129.9	18	133.0	18	131.2	18	67.7	41.9	49.6	35.8	52.0	19.4	44.1	53.6	90.5	34.0	115.2	158.2	46.6	35.6	175.0	205.5	17.3	19.5
32	17	130.1	16	133.1	16	131.2	16	68.2	41.9	50.3	36.2	51.8	19.7	44.7	54.5	92.3	33.3	115.5	159.9	46.6	33.9	176.7	211.7	17.3	19.5
33	29	131.1	17	133.5	17	131.3	17	68.5	42.7	50.7	36.3	52.1	19.8	44.9	53.1	92.9	33.4	115.9	160.2	47.9	35.1	177.8	214.5	17.2	19.7
34	16	130.7	15	133.3	15	131.4	15	67.9	42.0	50.7	36.2	52.0	19.6	44.7	55.5	92.4	33.3	115.5	159.3	46.9	33.8	176.9	212.6	17.1	19.4
35	17	130.6	17	133.5	17	131.5	17	68.5	42.7	50.7	36.2	52.3	19.7	44.6	55.4	93.1	34.0	115.8	160.5	47.1	35.3	176.0	211.1	17.2	19.6
36	30	131.6	15	133.7	15	131.8	15	68.4	40.6	50.7	35.9	52.1	19.7	44.4	53.7	94.9	32.9	117.8	162.6	47.0	35.2	174.7	206.8	17.2	19.6

TABLE 17.10. AVERAGE BODY WEIGHTS FOR GIVEN CHEST GIRTHS*

Weight in Pounds

Chest Girth (In)	Nebraska										Missouri						Grand Av.	
	Holstein		Jersey		Guernsey		Ayrshire		Average		Holstein		Jersey		Average			
	Obs.*	Com.†	Obs.	Com.	Obs.	Com.	Obs.	Com.	Obs.	Com.	Obs.	Com.	Obs.	Com.	Obs.	Com.	Obs.	Com.
22.5	—	—	41	38	—	—	—	—	41	39	—	—	—	—	—	38	41	39
23.5	53	48	42	43	—	—	—	—	47	44	—	—	41	41	41	43	45	44
24.5	67	54	54	49	49	45	63	46	55	50	—	—	—	47	—	48	55	50
25.5	—	60	53	55	60	50	65	51	55	56	—	—	51	52	51	54	54	56
26.5	70	66	59	61	63	56	66	57	61	62	54	62	55	58	54	60	60	62
27.5	82	74	63	68	69	63	69	64	68	69	64	69	62	65	62	67	67	69
28.5	89	81	72	75	72	70	77	71	78	76	73	76	67	72	68	74	75	76
29.5	90	89	75	83	78	77	79	78	83	84	83	84	71	79	75	81	81	84
30.5	93	99	84	91	81	85	84	86	88	92	87	92	83	87	85	90	87	92
31.5	102	107	92	99	90	93	86	94	96	101	96	101	91	96	94	98	95	101
32.5	110	116	106	109	103	102	100	103	107	110	103	111	101	105	102	107	105	110
33.5	114	127	115	118	95	111	110	113	112	120	111	120	112	114	111	117	112	120
34.5	125	137	125	129	127	121	114	123	124	130	118	131	122	124	120	127	123	130
35.5	129	148	141	139	113	132	115	133	129	141	147	142	136	135	141	138	134	141
36.5	153	160	144	151	147	143	136	144	147	153	149	154	141	146	146	150	147	153
37.5	160	172	167	163	139	155	146	156	157	165	159	166	160	167	159	162	158	165
38.5	166	186	184	175	166	167	142	168	168	178	176	179	172	170	174	174	170	178
39.5	192	199	199	188	184	190	182	181	191	191	204	192	196	183	201	187	195	191
40.5	207	213	192	202	174	194	193	195	199	205	219	207	203	196	212	201	204	205
41.5	225	228	247	217	201	208	214	209	225	219	225	221	218	210	222	216	224	219
42.5	238	243	234	232	228	223	208	224	233	234	244	237	233	225	240	231	235	235
43.5	250	259	246	248	234	238	231	239	242	250	263	253	250	241	256	247	246	250
44.5	277	276	287	264	249	254	265	256	276	267	278	270	269	257	274	264	275	267
45.5	295	293	297	281	268	271	294	272	292	284	296	288	288	274	293	281	292	284
46.5	314	312	311	299	293	289	269	290	306	302	308	306	300	291	305	299	305	302
47.5	326	330	328	318	318	308	313	308	323	320	338	325	321	310	329	317	326	321
48.5	352	350	350	337	340	327	333	327	348	339	356	345	336	329	348	337	348	340
49.5	367	370	371	357	359	347	347	347	363	359	381	366	346	348	370	357	362	361
50.5	389	391	390	377	373	367	390	368	388	380	405	387	372	369	391	378	389	382
51.5	428	412	411	399	419	389	395	389	419	402	423	409	395	390	408	400	415	403
52.5	445	435	439	421	427	411	413	411	434	424	448	432	413	412	430	422	433	426
53.5	480	458	456	444	450	435	446	434	463	447	467	456	431	435	450	446	458	449
54.5	502	482	472	468	464	458	485	458	486	471	497	481	457	459	482	470	485	473
55.5	525	506	499	493	497	483	493	483	508	496	512	506	481	484	496	495	503	498
56.5	546	532	536	518	518	509	519	508	535	521	546	532	498	509	525	521	532	523
57.5	581	558	546	545	532	536	549	535	557	548	566	560	498	535	533	548	548	550
58.5	591	585	576	572	551	563	556	562	575	575	590	588	535	562	559	575	570	578
59.5	629	613	598	600	587	592	606	590	611	603	618	617	576	590	599	604	607	606
60.5	655	642	630	629	641	621	618	619	639	632	648	647	609	619	630	633	636	635
61.5	675	671	659	659	664	651	647	649	664	661	659	677	637	649	647	664	659	665
62.5	713	702	689	689	698	683	682	680	797	692	698	709	668	679	684	695	693	696
63.5	744	733	731	711	698	715	714	711	731	723	734	742	720	711	726	727	730	728
64.5	772	765	772	754	695	748	752	744	765	756	781	776	765	743	771	760	766	761
65.5	816	798	799	787	762	782	770	777	798	789	804	810	794	776	797	794	798	794
66.5	846	832	820	821	835	817	812	812	829	823	853	846	817	811	826	829	828	829
67.5	884	867	844	857	836	854	840	848	853	859	884	883	870	846	873	866	860	865
68.5	914	902	882	893	903	891	893	885	897	897	908	920	898	883	900	903	898	901
69.5	945	939	913	930	922	929	946	923	931	932	962	959	930	920	939	941	933	939
70.5	983	977	948	969	984	968	977	961	970	970	1017	999	964	959	982	980	974	977
71.5	1036	1015	982	1008	976	1009	1006	1001	1009	1009	1061	1039	1016	998	1037	1020	1018	1017
72.5	1066	1054	1007	1048	1032	1050	1038	1042	1044	1049	1097	1081	1023	1038	1065	1061	1052	1057
73.5	1109	1095	1038	1090	1079	1093	1072	1084	1091	1091	1128	1124	1061	1080	1108	1104	1096	1100
74.5	1155	1137	1055	1133	1150	1137	1100	1127	1138	1133	1169	1169	1115	1123	1161	1147	1146	1142
75.5	1194	1178	1073	1175	1175	1181	1139	1171	1182	1176	1199	1213	1145	1166	1198	1191	1186	1185
76.5	1234	1222	1025	1221	1188	1228	1194	1216	1227	1220	1223	1260	1132	1211	1220	1238	1225	1231
77.5	1277	1266	—	—	1171	1275	1208	1262	1271	1266	1245	1307	1196	1257	1244	1284	1266	1276
78.5	1320	1312	—	—	1160	1324	1197	1310	1318	1312	1311	1356	—	—	1311	1332	1317	1324
79.5	1374	1359	—	—	—	—	1278	1359	1373	1360	1362	1406	—	—	1362	1381	1372	1372
80.5	1391	1406	—	—	—	—	1386	1408	1391	1408	1365	1456	—	—	1365	1431	1389	1421
81.5	1426	1454	—	—	—	—	1377	1460	1426	1458	1407	1509	—	—	1407	1483	1425	1472
82.5	1472	1504	—	—	—	—	1356	1512	1471	1509	1358	1562	—	—	1358	1535	1470	1523
83.5	1484	1554	—	—	—	—	—	—	1484	1560	1535	1616	—	—	1535	1589	1485	1575
84.5	1542	1606	—	—	—	—	—	—	1542	1614	1577	1672	—	—	1577	1644	1543	1630
85.5	1598	1659	—	—	—	—	—	—	1598	1668	—	—	—	—	—	—	1598	1684
86.5	1676	1712	—	—	—	—	—	—	1676	1723	—	—	—	—	—	—	1676	1740
87.5	1676	1767	—	—	—	—	—	—	1676	1779	—	—	—	—	—	—	1676	1797
88.5	1697	1823	—	—	—	—	—	—	1697	1837	—	—	—	—	—	—	1697	1856
89.5	1776	1880	—	—	—	—	—	—	1776	1895	—	—	—	—	—	—	1776	1916
90.5	1861	1938	—	—	—	—	—	—	1861	1955	—	—	—	—	—	—	1861	1976
91.5	—	1998	—	—	—	—	—	—	—	2017	—	—	—	—	—	—	—	2038
92.5	1865	2058	—	—	—	—	—	—	1865	2079	—	—	—	—	—	—	1865	2102

* Observed geometric averages.

† Computed from equation $Y = aX^n$.

TABLE 17.11. CHEST GIRTH, AGE, WEIGHT RELATIONSHIPS—HOLSTEIN FEMALES

Live weights in pounds

Chest girth (in)	Age in months																		
	Birth	1	2	3	4	5	6	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24
23	69																		
24	72	73																	
25	75	77																	
26	79	80																	
27	82	84	99																
28	85	88	104																
29	88	91	109																
30	92	95	114	132															
31	95	98	118	139															
32	98	102	123	145															
33	102	106	128	152	165														
34	105	109	133	158	174														
35	108	113	138	165	182														
36	111	116	143	172	190	199													
37	115	120	148	179	198	209													
38		124	154	186	207	219	229												
39		128	159	193	215	229	241												
40		131	164	200	224	240	253	258											
41			169	208	233	250	265	271											
42			175	215	242	261	277	284											
43			180	222	251	272	289	297	316										
44			186	230	261	284	302	310	330										
45				237	270	295	315	324	345	350									
46				245	280	307	328	338	360	366	381								
47				253	289	319	341	352	375	381	398								
48				260	299	331	355	367	391	397	414	424							
49					309	343	369	382	407	413	430	441	452						
50					319	356	383	397	424	430	447	458	469	484					
51					329	368	398	413	440	446	464	476	487	502					
52						381	413	429	457	463	481	493	507	520	534				
53						394	428	445	474	481	499	511	523	539	554				
54						408	443	461	492	498	517	529	542	558	573	584			
55							458	478	510	516	536	548	561	577	593	604			
56							474	495	528	535	555	567	580	596	613	624	631		
57							490	512	547	553	574	586	599	616	633	645	653		
58							506	530	566	572	593	605	619	636	653	667	676		
59								548	585	591	613	625	639	656	674	689	698	706	
60								566	604	611	633	645	660	677	696	711	721	729	
61								584	624	631	653	666	680	698	717	733	745	753	759
62								603	644	651	673	686	701	719	739	756	769	778	785

Chest girth (in)	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24	25 to 28	29 to 32	33 to 36	37 to 42	43 to 48	49 to 54	55 to 60	61 to 72	73 and over
63	664	671	694	707	722	740	761	779	793	803	811	816								
64	685	692	716	728	744	762	783	802	817	828	837	844	852							
65	706	713	737	750	766	784	806	825	841	853	863	872	879	893						
66		734	759	772	788	806	829	849	866	879	890	900	907	922	931					
67		756	781	794	811	829	852	873	891	905	918	928	936	950	960	966				
68		778	804	816	834	852	876	898	916	932	946	956	966	979	989	995	1006			
69			826	839	857	875	900	922	942	959	974	985	996	1009	1018	1024	1036	1049		
70			849	862	880	899	924	947	968	988	1003	1015	1026	1040	1048	1054	1066	1079	1092	
71				886	904	923	948	973	996	1016	1033	1046	1057	1071	1079	1084	1096	1109	1122	1126
72					928	947	973	998	1023	1044	1062	1077	1088	1101	1109	1115	1126	1137	1151	1156
73						971	998	1024	1051	1072	1092	1108	1120	1132	1140	1146	1157	1169	1180	1187
74						995	1023	1050	1079	1101	1122	1139	1152	1164	1172	1177	1188	1199	1211	1218
75							1049	1077	1107	1131	1153	1171	1184	1196	1204	1210	1219	1230	1242	1249
76							1074	1105	1135	1161	1184	1204	1217	1229	1236	1242	1251	1262	1274	1280
77								1133	1164	1191	1216	1237	1251	1262	1270	1274	1284	1294	1306	1311
78								1160	1194	1222	1248	1271	1285	1296	1303	1308	1316	1327	1348	1343
79									1223	1253	1280	1305	1319	1330	1337	1341	1349	1358	1368	1376
80									1253	1285	1313	1339	1353	1364	1371	1375	1383	1393	1403	1408
81										1317	1346	1373	1390	1399	1406	1410	1417	1425	1436	1440
82										1349	1380	1408	1425	1435	1441	1444	1451	1459	1469	1474
83											1414	1444	1462	1472	1476	1480	1486	1493	1503	1508
84											1449	1481	1499	1509	1512	1516	1521	1527	1535	1542
85												1519	1536	1545	1548	1551	1556	1563	1571	1576
86												1556	1574	1582	1585	1588	1592	1599	1307	1610
87													1612	1620	1622	1625	1628	1633	1641	1645
88														1658	1660	1663	1665	1671	1675	1680
89															1698	1700	1702	1706	1710	1716
90															1736	1738	1740	1742	1746	1752
91																1777	1778	1782	1783	1789
92																	1816	1819	1820	1826
93																		1858	1858	1863
94																			1897	1899
95																				1936

TABLE 17.12. CHEST GIRTH, AGE, WEIGHT RELATIONSHIPS—JERSEY FEMALES

Chest girth (in)	Age in months																				
	Birth	1	2	3	4	5	6	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24		
20	39																				
21	41																				
22	44	47																			
23	46	50																			
24	49	53	64																		
25	52	56	68																		
26	54	60	72	83																	
27	57	63	76	88																	
28	60	66	80	93	108																
29	62	69	84	98	114																
30	65	72	88	103	120	134															
31	68	76	92	108	127	141															
32	71	79	96	114	133	149	162														
33	74	82	101	119	140	156	171														
34	76	86	105	124	146	164	180	188													
35	79	89	109	130	153	172	188	198													
36	82	93	114	136	160	180	197	207													
37		96	118	141	167	188	206	217													
38		100	123	147	174	196	216	227	236												
39			128	153	181	204	225	237	247												
40			132	159	189	213	234	247	258	267											
41			137	165	196	222	244	258	269	279											
42			142	171	204	230	254	268	280	291	298										
43				177	211	239	264	279	292	303	311										
44				184	219	248	274	290	304	315	324	333									
45					227	257	284	301	316	327	337	346									
46					235	266	295	313	328	340	350	360	366								
47					243	276	305	324	340	353	363	373	380								
48						285	316	336	352	366	376	387	394	406							
49						295	327	348	365	379	390	401	409	420							
50						305	338	360	378	383	404	416	424	435	451						
51						315	439	372	391	407	418	430	438	450	466	482					
52							360	384	404	421	433	445	453	465	482	498	512				
53							372	397	418	435	447	460	468	481	498	514	528	541			
54							394	409	431	449	462	475	484	496	514	530	545	558	564		

Live weights in pounds

Chest girth (in)	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24	25 to 28	29 to 32	33 to 36	37 to 42	43 to 48	49 to 54	55 to 60	61 to 72	73 and over
55	422	445	463	477	491	499	512	530	547	562	576	582	582								
56	435	459	478	492	506	515	528	546	563	579	593	601	602	602							
57	448	473	493	508	522	531	544	562	580	596	611	620	622	623	627						
58	461	487	508	523	538	547	560	579	597	613	629	639	642	644	648	654					
59		502	523	539	555	564	577	596	614	631	648	658	663	666	670	676	687				
60		516	539	555	571	580	594	613	632	649	667	678	684	688	692	698	708	713			
61		531	554	571	588	597	611	630	649	667	686	698	705	710	714	720	730	735	735		
62			570	588	605	614	628	647	667	685	705	718	726	732	737	742	752	757	758	758	
63			586	604	622	631	646	665	685	703	724	738	748	755	760	765	775	780	781	781	781
64				621	639	649	663	683	703	722	744	759	771	778	784	789	799	803	804	805	805
65				638	656	666	681	701	721	741	763	780	793	802	808	812	822	827	828	829	830
66					674	684	699	719	740	760	783	801	816	826	832	836	846	851	852	854	855
67					692	703	717	738	759	779	804	822	839	850	856	861	870	875	876	879	880
68						721	736	756	778	798	824	844	862	874	881	886	894	899	900	904	905
69						739	754	775	797	818	844	866	885	899	906	910	918	924	925	930	931
70							773	794	816	838	865	888	909	924	932	936	943	949	950	956	957
71							792	813	836	858	886	910	934	950	958	962	969	974	976	982	984
72								832	855	878	907	932	958	976	984	988	994	1000	1002	1009	1011
73								852	875	898	929	955	983	1002	1010	1014	1020	1026	1028	1036	1038
74									895	919	950	978	1008	1028	1037	1041	1046	1052	1054	1063	1066
75										940	972	1002	1033	1055	1064	1068	1073	1079	1081	1091	1094
76										960	994	1025	1059	1082	1092	1095	1099	1106	1108	1119	1122
77											1016	1049	1085	1110	1120	1123	1126	1133	1136	1148	1151
78												1073	1111	1138	1148	1151	1154	1160	1164	1176	1180
79													1137	1166	1177	1179	1182	1188	1192	1205	1209
80														1195	1206	1208	1210	1216	1220	1235	1239
81														[illegible]	1235	1237	1238	1245	1249	1265	1269
82																1266	1266	1274	1278	1295	1299
83																	1295	1303	1307	1326	1330
84																		1332	1337	1357	1361
85																			1367	1387	1391

TABLE 17.13. CHEST GIRTH, AGE, WEIGHT RELATIONSHIPS—GUERNSEY FEMALES

Chest girth (in)	Age in months																		
	Birth	1	2	3	4	5	6	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24
20	38																		
21	41	43																	
22	44	46	50																
23	47	49	54																
24	50	53	58	66															
25	54	56	62	70															
26	57	60	66	75	85														
27	60	64	70	80	91														
28	64	68	75	85	97														
29	**67**	72	79	91	103	117													
30	71	**76**	84	96	110	124													
31	75	80	89	102	116	131	145												
32	78	84	93	107	123	139	153												
33	82	89	**98**	113	130	147	162												
34	86	93	103	119	137	155	171	181											
35	90	97	108	125	144	163	179	190											
36	94	102	114	132	151	171	188	199											
37		107	119	**138**	159	180	198	209	224										
38		111	124	144	166	188	207	219	235										
39		116	130	151	174	197	217	229	246	251									
40		121	135	158	**182**	206	226	239	257	263									
41			141	165	190	215	236	249	268	275	278								
42			147	172	198	225	246	260	279	287	291								
43			153	179	207	**234**	257	270	291	300	304	306							
44				186	216	244	267	281	303	313	318	320							
45				193	224	254	278	292	315	326	332	335	341						
46				201	233	264	**289**	303	327	339	346	350	357						
47					242	274	300	315	339	352	360	365	372	380					
48					251	285	311	326	352	365	375	380	388	396					
49					260	295	322	**338**	364	379	390	395	405	412					
50						306	334	350	377	393	405	411	422	429	447				
51						317	345	362	**390**	408	420	427	439	446	464				
52						328	357	374	404	422	436	444	456	463	481				
53						339	369	386	417	**437**	452	461	473	480	498	517			
54							381	399	431	452	468	478	491	498	516	534			
55							394	412	445	467	485	495	509	516	534	552	562		
56							406	425	459	482	502	**513**	528	534	552	571	580		
57								438	473	498	519	531	547	553	570	589	599	612	
58								451	488	514	536	549	**566**	572	589	608	619	632	
59								464	503	530	**554**	568	586	**592**	608	627	638	653	661

Live weights in pounds

Chest girth (in)			8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24	25 to 28	29 to 32	33 to 36	37 to 42	43 to 48	49 and over
60			517	546	571	587	607	611	627	647	658	674	683	704					
61			532	562	589	606	627	631	647	666	678	695	706	729	744				
62			547	579	608	626	648	652	**667**	686	699	716	729	754	770	774			
63				596	627	645	669	672	687	706	719	738	753	779	796	800	807		
64				613	646	665	690	693	707	**727**	740	760	777	805	822	826	833	843	
65					665	686	712	714	728	747	**761**	782	801	832	848	852	839	870	883
66						706	734	736	749	768	783	804	825	859	875	879	886	897	910
67							757	758	770	790	805	**827**	850	886	903	907	913	925	938
68								780	791	811	827	850	876	914	931	934	940	953	966
69									813	833	849	874	**901**	**942**	959	962	968	981	995
70									835	855	871	898	927	971	**988**	991	997	1010	1024
71										877	894	922	954	1000	1017	**1020**	1026	1039	1054
72										899	917	946	980	1029	1046	1049	**1055**	1068	1084
73											940	970	1007	1059	1076	1079	1085	**1098**	1114
74												995	1035	1090	1107	1109	1115	1128	**1145**
75												1020	1063	1121	1138	1140	1146	1159	1176
76													1091	1152	1169	1171	1177	1190	1207
77														1183	1201	1202	1208	1221	1239
78															1233	1234	1239	1253	1271
79																	1271	1285	1304
80																		1317	1337
81																			1370

TABLE 17.14. CHEST GIRTH, AGE, WEIGHT RELATIONSHIPS—AYRSHIRE FEMALES

Chest girth (in)	Age in months																		
	Birth	1	2	3	4	5	6	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24
21	45																		
22	48																		
23	52	52																	
24	55	56																	
25	58	59	67																
26	62	62	71																
27	65	66	75	89															
28	68	70	80	94															
29	72	74	84	100															
30	76	78	89	106	122														
31	79	82	94	112	129														
32	83	86	99	118	136														
33	87	90	104	124	143	153									Live weights in pounds				
34	90	94	109	130	151	162													
35	94	98	114	137	159	171													
36	98	102	119	143	167	180	192												
37	102	107	125	150	175	189	202												
38	106	111	130	157	183	198	213												
39		116	136	164	192	208	223	233											
40		120	141	171	201	218	234	245											
41		125	147	178	209	228	245	256											
42		130	153	185	218	238	256	268	279										
43		134	158	193	227	248	268	281	293										
44			164	200	237	258	279	293	306	312									
45			170	208	246	269	291	306	320	326									
46			177	216	256	280	303	319	334	341	347								
47			184	224	265	291	316	333	348	356	362								
48			190	232	275	303	328	346	363	371	377	385							
49				240	285	314	341	360	378	387	393	401							
50				248	296	326	354	375	393	402	409	417	429						
51				256	306	338	368	389	409	418	425	433	446						
52				265	316	350	381	404	425	435	442	450	462	477					
53					327	362	395	419	441	452	459	467	479	495					
54					338	374	409	434	457	469	476	484	496	512	524				
55					349	387	423	449	474	486	494	502	514	530	543				
56					360	400	437	465	491	503	512	520	532	548	561	568			
57						413	452	481	509	521	530	538	550	567	580	588	604		
58						426	467	497	526	540	548	556	568	586	599	608	625		
59							482	514	544	558	567	575	587	605	619	628	646	660	
60							497	531	562	577	586	594	606	624	639	648	667	682	684
Chest girth (in)		7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24	25 to 28	29 to 32	33 to 36	37 to 42	43 to 48	49 and over
61		548	581	596	605	613	625	643	659	669	688	704	707	709					
62		565	600	616	625	633	644	663	679	690	710	727	730	733	733				
63			619	636	645	653	664	683	700	711	732	750	754	757	758	777			
64				656	665	673	684	704	721	732	755	774	778	782	784	804	815		
65					686	694	705	724	742	754	778	797	802	807	811	832	844	847	
66					707	715	725	745	764	776	801	821	827	832	838	860	874	878	881
67						736	746	767	786	799	824	846	852	858	865	889	904	909	913
68						757	767	788	808	822	848	871	878	885	892	918	935	940	946
69							789	810	830	845	872	896	904	912	920	948	966	972	978
70							811	832	853	868	896	922	930	939	949	979	998	1005	1012
71								854	876	892	921	948	957	966	979	1010	1030	1039	1046
72									900	916	946	974	984	994	1008	1041	1063	1073	1081
73										940	971	1001	1011	1022	1038	1073	1096	1108	1117
74										964	997	1028	1039	1051	1069	1106	1130	1144	1154
75											1023	1056	1067	1081	1100	1139	1165	1180	1191
76											1049	1083	1095	1110	1131	1172	1200	1217	1229
77												1111	1124	1140	1163	1206	1236	1255	1268
78													1153	1170	1195	1240	1273	1293	1307
79													1182	1201	1228	1275	1310	1332	1346
80														1232	1262	1311	1348	1371	1386
81															1295	1347	1386	1411	1427
82																1384	1424	1451	1468
83																	1463	1492	1510
84																		1534	1552
85																			1595

TABLE 17.15. RELATION BETWEEN LIVE WEIGHT AND HEIGHT AT WITHERS OF DAIRY CATTLE

Heights at withers (in)	Live weights in pounds				
	Holstein	Jersey	Guernsey	Ayrshire	Average
22	—	—	—	30	—
22½	—	—	—	33	—
23	34	34	—	37	—
23½	38	38	—	40	—
24	41	41	39	44	41
24½	45	45	43	48	45
25	49	49	47	52	49
25½	52	54	51	57	54
26	57	58	56	62	58
26½	62	63	61	67	63
27	68	69	66	73	69
27½	73	74	71	79	74
28	79	81	77	85	80
28½	85	87	84	92	87
29	91	94	90	99	94
29½	98	101	97	107	101
30	106	109	105	115	109
30½	113	117	113	123	116
31	121	126	122	132	125
31½	130	135	130	142	134
32	139	144	140	152	144
32½	148	154	150	162	154
33	158	165	160	173	164
33½	168	176	171	185	175
34	179	188	183	197	187
34½	191	200	195	210	199
35	203	213	208	223	212
35½	215	226	222	237	225
36	228	240	236	252	239
36½	242	255	251	268	254
37	257	271	267	284	270
37½	272	287	283	301	286
38	287	304	300	319	302
38½	304	322	318	337	320
39	321	341	337	356	339
39½	338	360	356	376	358
40	357	380	377	397	378
40½	376	401	398	419	398
41	396	423	420	442	420
41½	417	446	443	465	443
42	439	470	468	490	467
42½	461	495	493	516	491
43	485	521	520	543	517
43½	509	548	547	570	544
44	534	576	575	598	571
44½	561	605	605	628	600
45	588	635	636	660	630
45½	616	667	668	692	661
46	645	699	701	726	693
46½	675	732	735	760	726
47	706	767	771	796	760
47½	739	803	808	833	796
48	772	740	846	871	832
48½	807	879	886	911	871
49	843	919	928	952	910
49½	880	961	971	995	952
50	918	1004	1015	1039	994
50½	958	1048	1061	1084	1038
51	999	1094	1108	1132	1083
51½	1041	1141	1157	1180	1130
52	1084	1190	1208	1230	1178
52½	1129	1242	1261	1282	1228
53	1175	1294	1315	1336	1280
53½	1223	1348	1371	1391	1333
54	1272	1403	1428	1447	1388
54½	1322	1460	1488	1506	1444
55	1375	1520	1550	1567	1503
55½	1428	—	1613	1629	—
56	1483	—	1679	1693	—
56½	1539	—	1746	1758	—
57	1597	—	1815	1826	—
57½	1657	—	—	—	—
58	1720	—	—	—	—
58½	1785	—	—	—	—
59	1850	—	—	—	—
59½	1917	—	—	—	—
60	1987	—	—	—	—
60½	2058	—	—	—	—
61	2130	—	—	—	—

TABLE 17.16. HEIGHT AT WITHERS AS RELATED TO AGE AND WEIGHT OF HOLSTEIN FEMALES

Height at withers (in)	Age in months																			
	Birth	1	2	3	4	5	6	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24	25 to 28
22	49																			
22½	52																			
23	54																			
23½	56																			
24	59	61																		
24½	62	64																		
25	65	67																		
25½	68	70																		
26	71	73	83																	
26½	74	77	86																	
27	77	80	90																	
27½	80	84	94																	
28	84	87	99	111																
28½	87	91	103	116																
29	90	94	108	122																
29½	94	98	112	127																
30	97	102	117	133	143															
30½	101	106	122	138	150															
31	104	110	126	144	157															
31½	108	114	131	150	164															
32	112	118	136	157	171	181														
32½	116	123	142	163	179	190														
33	120	127	147	170	186	198														
33½	124	132	152	176	194	207														
34	128	136	158	183	203	216	227													
34½		141	164	190	211	225	236													
35		146	170	197	220	234	246	263												
35½		150	176	205	228	244	257	274												
36		155	182	212	237	254	267	285												
36½			188	220	247	264	278	296												
37			194	228	256	275	289	308	321											
37½			200	236	266	286	301	320	333											
38			207	244	276	297	313	333	346	360										
38½			214	252	286	308	325	346	359	373										
39			220	261	296	320	337	359	372	387	399									
39½				270	307	332	350	372	386	401	413									
40				279	318	344	363	386	400	415	428	445								
40½				288	329	356	376	399	414	430	443	460								
41				297	340	369	389	414	429	445	458	475	496							
41½				306	352	382	403	428	444	460	473	490	511							
42				316	364	395	417	443	459	475	489	506	527	548						
42½					376	409	432	459	475	491	505	522	543	564						
43					388	423	447	474	491	508	521	538	560	581	611					
43½					401	438	462	490	507	524	538	554	576	597	628					
44					414	452	477	507	524	541	555	571	593	614	645	681				
44½						467	493	524	541	558	572	589	611	631	662	698				
45						482	509	541	558	576	590	606	628	648	679	716	745			
45½						498	526	558	576	594	608	624	646	666	696	734	763			
46						514	543	576	594	612	627	642	664	684	714	752	781	809		
46½							560	594	613	631	645	660	682	702	732	770	799	828		
47							577	612	632	650	664	679	701	721	751	788	818	847	871	903
47½								631	651	669	684	699	720	739	769	807	837	866	890	922

Live weights in pounds

Height at withers (in)	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24	25 to 28	29 to 32	33 to 36	37 to 42	43 to 48	49 to 54	55 to 60	61 to 72	73 and over
48	650	670	689	704	817	740	758	788	826	856	885	909	941	985	1029	1072	1120				
48½		690	709	724	738	760	778	807	845	875	905	929	961	1005	1048	1090	1137				
49		710	730	745	758	780	797	826	865	894	925	949	981	1025	1068	1109	1154	1192	1228	1264	1271
49½			751	766	779	800	817	846	885	914	945	969	1001	1045	1087	1128	1171	1208	1243	1279	1287
50			772	787	800	821	838	866	905	934	965	990	1022	1066	1107	1147	1189	1224	1259	1294	1302
50½				808	821	842	858	886	925	954	985	1010	1042	1086	1127	1165	1206	1241	1275	1310	1317
51				830	842	863	879	907	945	974	1006	1031	1063	1107	1147	1184	1224	1257	1291	1325	1332
51½					864	885	900	927	966	995	1027	1052	1084	1127	1167	1203	1241	1273	1306	1340	1348

TABLE 17.16.—*Continued*

Height at withers (in)	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24	25 to 28	29 to 32	33 to 36	37 to 42	43 to 48	49 to 54	55 to 60	61 to 72	73 and over
52					886	907	921	948	987	1016	**1048**	1073	1106	1148	1187	1222	1259	1290	1322	1356	1363
52½						929	943	969	1008	1037	1069	**1095**	1127	1170	1208	1242	1277	1306	1338	1371	1378
53						952	965	991	1029	1058	1091	1117	**1149**	1191	1228	1262	1295	1321	1354	1386	1394
53½							987	1013	1051	1080	1112	1139	1171	**1212**	1249	1281	1313	1340	1370	1402	1409
54							1010	1035	1073	1101	1134	1161	1193	1234	**1270**	1300	1331	1356	1386	1417	1424
54½								1057	1095	1123	1156	1183	1215	1256	1291	**1320**	**1349**	**1373**	**1402**	1433	1440
55								1079	1118	1145	1179	1206	1238	1278	1312	1341	1368	1390	1418	1448	1456
55½									1140	1168	1201	1228	1260	1300	1333	1360	1386	1406	1434	1464	1471
56									1163	1190	1224	1251	1283	1323	1354	1380	1404	1423	1450	1479	1486
56½										1213	1247	1274	1306	1345	1376	1401	1422	1440	1466	1495	1501
57										1236	1271	1298	1330	1368	1398	1421	1441	1457	1482	1511	1517
57½											1294	1322	1353	1391	1420	1442	1460	1474	1499	1526	1533
58											1317	1346	1377	1414	1442	1462	1479	1491	1515	1542	1548
58½													1401	1438	1464	1483	1498	1508	1532	1558	1564
59													1425	1461	1486	1504	1516	1525	1548	1573	1580
59½															1509	1525	1535	1543	1565	1589	1596
60															1532	1546	1555	1560	1582	1605	1612
60½																		1578	1598	1621	1627
61																		1595	1614	1636	1643
61½																				1652	1658
62																				1668	1674

TABLE 17.17. HEIGHT AT WITHERS AS RELATED TO AGE AND WEIGHT OF JERSEY FEMALES

Live weights in pounds

Height at withers (in)	Age in months																			
	Birth	1	2	3	4	5	6	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24	25 to 28
22	38																			
22½	40																			
23	42	46																		
23½	44	48																		
24	47	51	57																	
24½	49	54	60																	
25	52	57	63																	
25½	54	60	67																	
26	57	63	70	81																
26½	60	66	74	86																
27	63	69	78	90																
27½	66	72	81	95																
28	69	76	85	99	111															
28½	72	79	89	104	116															
29	75	83	94	109	122															
29½	78	87	98	114	128															
30	81	91	102	120	134	144														
30½		95	107	125	140	151														
31		99	112	131	146	158	171													
31½		103	116	137	153	165	179													
32		107	121	143	160	173	187	196												
32½		111	126	149	167	180	195	205												
33		116	132	155	174	188	204	214	223											
33½			137	162	181	196	212	223	233											
34			142	168	189	204	221	233	243	250										
34½			148	175	196	213	231	243	253	261										
35			154	182	204	222	240	253	264	272	283									
35½				189	212	231	250	263	275	283	294									
36				196	221	240	260	274	286	294	306	318								
36½				204	229	249	270	285	298	306	318	330								
37				212	238	258	280	296	309	318	330	342	358	388						
37½					247	268	291	307	321	330	342	355	370	400						
38					256	278	302	319	334	343	355	367	383	413	446					
38½					265	288	314	331	347	356	368	380	396	425	458					
39					275	299	325	344	360	369	382	394	409	438	470	503				
39½						310	337	356	373	383	395	407	422	450	482	514				
40						321	349	369	387	397	409	421	435	463	494	525	555			
40½						332	361	382	401	411	423	435	449	476	507	537	566			
41						343	374	396	415	425	438	449	463	490	519	549	577	605		
41½							387	410	429	440	453	463	477	504	532	561	588	616		
42							400	424	444	455	468	478	491	518	545	573	600	627	645	663
42½							413	438	459	471	484	494	506	532	558	585	611	638	657	675

Height at withers (in)	6	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24	25 to 28	29 to 32	33 to 36	37 to 42	43 to 48	49 to 54	55 to 60	61 to 72	73 and over
43	427	453	475	487	500	509	522	546	571	597	623	649	668	687	715	740	760	769				
43½		468	491	503	516	525	537	560	585	609	634	660	679	699	728	753	774	783				
44		483	507	519	532	541	552	575	598	622	646	671	690	711	741	767	788	798	809	821	837	839
44½		499	523	536	549	558	568	590	612	635	658	683	702	724	754	781	803	813	824	837	852	854
45		515	540	553	566	574	584	605	626	647	670	694	713	736	767	795	817	828	839	852	867	870
45½			558	571	584	591	600	620	640	660	682	705	725	748	780	809	832	843	855	868	883	885
46			576	589	602	608	617	636	654	673	694	716	736	761	793	823	847	858	870	883	899	901
46½				607	620	626	634	651	668	686	706	728	748	773	807	837	862	873	886	899	914	916
47				626	639	644	651	667	683	699	718	739	760	786	820	851	877	889	901	915	929	932
47½					658	662	669	683	697	712	730	751	771	799	834	866	892	904	917	931	945	948
48					677	681	686	700	712	725	742	762	783	811	847	880	907	920	933	947	961	963
48½						700	704	716	727	739	755	774	795	824	861	895	923	935	949	963	977	979
49						719	723	733	742	752	767	786	807	837	875	909	938	951	965	979	993	996
49½						738	741	750	757	766	780	797	819	850	889	924	954	967	981	995	1009	1012
50						758	760	767	773	780	793	809	831	863	903	939	970	983	998	1012	1026	1028
50½							779	785	788	794	805	821	843	876	917	954	985	999	1014	1028	1042	1044
51							798	803	804	808	818	833	855	889	931	969	1001	1015	1031	1045	1059	1061
51½								820	820	822	831	845	867	902	945	984	1017	1031	1047	1062	1075	1078
52								838	836	837	844	857	880	916	959	999	1033	1048	1064	1079	1092	1094
52½									852	852	857	869	892	929	974	1014	1049	1064	1081	1096	1108	1111
53										867	870	881	904	942	988	1030	1066	1081	1098	1113	1125	1128
53½												893	917	956	1003	1045	1082	1098	1115	1130	1142	1145
54														969	1017	1060	1098	1114	1132	1147	1159	[illegible]
54½																1076	1115	1131	1149	1164	1176	1179
55																		1148	1167	1182	1194	1196

Table 17.18. Height at Withers as Related to Age and Weight of Guernsey Females

Live weights in pounds

Height at withers (in)	Age in months																		
	Birth	1	2	3	4	5	6	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24
23	42																		
23½	44	46																	
24	47	49	54																
24½	50	52	57	65															
25	52	55	60	69															
25½	55	58	64	73															
26	58	61	67	77	85														
26½	61	64	71	81	90														
27	64	67	75	86	95														
27½	**67**	71	79	90	100														
28	70	74	83	95	105	117													
28½	74	**78**	87	100	111	123													
29	77	82	92	105	117	129	140												
29½	81	86	96	111	123	136	147												
30	84	90	**101**	116	129	143	155	162											
30½	88	94	106	122	135	150	162	170											
31	92	98	111	128	142	157	170	178	189										
31½	96	103	116	134	149	164	178	187	198										
32	100	107	121	**140**	156	172	186	195	207	214									
32½		112	126	146	163	180	195	204	216	224									
33		117	132	153	170	188	203	213	225	234	234								
33½		121	137	160	178	197	212	222	235	244	244								
34		126	143	167	**186**	205	221	231	245	255	255	258							
34½			149	174	194	214	231	241	255	265	266	269							
35			156	181	202	223	241	251	265	276	277	281	288						
35½			162	189	211	**233**	251	261	276	288	289	293	300						
36			169	196	220	242	261	272	287	299	301	305	313	319					
36½				204	229	252	271	283	298	311	313	317	326	332					
37				212	238	262	282	294	310	324	325	330	339	345	357				
37½				221	247	273	**293**	305	322	336	338	343	353	359	371				
38				229	257	283	305	316	334	349	351	357	367	374	385	413			
38½					267	294	316	328	347	362	365	371	381	389	400	428			
39					278	306	328	**340**	359	376	378	385	396	404	415	**444**	469		
39½					288	317	340	352	372	389	392	400	411	419	431	459	484		
40					299	329	353	365	386	403	407	415	427	435	447	475	500	527	
40½						341	366	378	**399**	418	422	430	443	451	463	491	516	544	
41						353	379	391	413	**433**	437	446	459	468	480	508	533	561	583
41½						366	392	405	427	448	452	462	476	485	497	525	550	578	600

Height at withers (in)	5	6	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24	25 to 28	29 to 32	33 to 36	37 to 42	43 to 48	49 and over
42	379	406	419	442	463	**468**	478	493	503	515	543	567	595	618	638					
42½		420	433	457	479	485	495	511	521	533	561	585	613	636	656					
43		434	447	472	495	501	**513**	529	539	551	579	603	631	654	674	706	742			
43½		449	462	488	512	518	530	547	558	570	597	621	649	673	693	725	762	797	821	
44		464	477	504	529	535	548	**566**	577	589	616	640	668	692	712	744	782	818	842	864
44½			493	520	546	553	567	585	**597**	609	635	659	687	711	731	764	802	839	863	886
45			508	536	563	571	586	605	617	629	655	678	706	731	751	784	823	860	884	908
45½			524	553	581	590	605	625	637	**650**	675	698	726	751	771	805	844	882	906	930
46			540	570	599	609	625	646	658	671	696	718	746	771	791	825	865	904	928	953
46½				588	618	628	645	667	679	692	**717**	738	766	791	812	846	886	926	950	975
47				606	637	648	665	688	701	714	738	**758**	787	812	833	867	908	948	973	998
47½				624	656	668	686	710	723	736	760	779	**808**	833	854	889	930	970	996	1022
48				643	676	688	707	732	746	758	782	800	829	**854**	875	910	952	993	1019	1045
48½					696	709	729	755	770	781	804	822	850	876	897	932	974	1016	1043	1069
49					716	730	752	778	793	805	827	844	872	899	**919**	**955**	**997**	**1040**	1067	1093
49½					737	752	775	802	817	829	850	867	894	921	941	978	1020	1064	**1091**	1118
50					758	774	798	826	842	854	874	890	917	944	964	1001	1044	1088	1115	**1143**
50½						796	821	851	868	879	898	913	940	967	987	1024	1068	1113	1140	1168
51						819	845	876	893	904	922	936	963	990	1011	1047	1092	1137	1165	1193
51½							870	902	919	930	947	960	987	1014	1034	1071	1116	1162	1190	1219
52								928	946	957	973	984	1011	1038	1058	1095	1141	1188	1216	1245
52½									973	984	998	1009	1035	1063	1083	1120	1166	1213	1242	1271
53											1024	1034	1060	1088	1107	1145	1191	1239	1268	1298
53½												1060	1085	1113	1132	1170	1217	1266	1295	1324
54														1138	1157	1195	1242	1292	1321	1351
54½																1221	1268	1319	1348	1379
55																		1346	1376	1407
55½																				1435

TABLE 17.19. HEIGHT AT WITHERS AS RELATED TO AGE AND WEIGHT OF AYRSHIRE FEMALES

Live weights in pounds

Height at withers (in)	Age in months																		
	Birth	1	2	3	4	5	6	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24
21	42																		
21½	44																		
22	46	48																	
22½	49	50																	
23	51	53																	
23½	53	55																	
24	55	58	61																
24½	57	61	65																
25	60	64	68	73															
25½	62	66	72	77															
26	64	69	75	82	86														
26½	67	72	79	86	91														
27	69	75	83	91	96														
27½	72	79	87	96	102														
28	74	82	91	101	108	110													
28½	77	85	95	107	114	116													
29	80	88	100	112	121	123													
29½	82	92	104	118	127	131													
30	85	95	109	124	134	138	141												
30½	88	99	114	130	142	146	150												
31	91	102	118	136	149	154	158	166											
31½	94	106	123	143	157	163	167	175											
32	96	110	128	149	165	171	176	184	193										
32½		114	134	156	173	181	185	194	203										
33		118	139	163	182	190	195	204	213	223									
33½		122	144	171	191	200	206	215	224	234									
34		126	150	178	200	210	216	226	236	245									
34½		130	156	186	209	220	227	237	247	257									
35		134	162	194	219	231	239	249	259	269	276								
35½			168	202	229	242	250	261	272	282	289								
36			174	211	239	254	262	274	284	295	302	311							
36½			180	219	250	266	275	287	298	308	315	324							
37			187	228	261	278	288	301	311	322	329	338							
37½			193	237	272	291	301	314	325	336	343	352							
38			200	246	284	304	315	329	340	351	358	367	376						
38½				256	296	318	329	344	355	366	373	382	392						
39				266	308	332	344	359	370	381	389	397	407						
39½				276	321	346	359	375	386	397	405	413	423						
40				286	334	361	375	391	403	414	421	429	439	454					
40½				296	347	376	391	407	419	430	438	445	456	471					
41				307	361	392	408	424	437	447	455	462	473	488	505				
41½					375	408	425	442	454	465	472	480	490	505	523				
42					389	425	442	461	473	484	490	498	508	523	541	561			
42½					404	442	460	480	492	503	509	516	527	542	559	579	600		
43					419	460	479	499	511	522	528	535	546	561	577	597	619	634	
43½						478	498	519	531	542	548	554	565	580	596	616	637	653	666

Height at withers (in)	5	6	7	8	9	10	11	12	13 and 14	15 and 16	17 and 18	19 and 20	21 and 22	23 and 24	25 to 28	29 to 32	33 to 36	37 to 42	43 to 48	49 and over
44	496	518	539	551	562	568	574	585	599	615	635	656	672	686	693	703				
44½	515	538	560	572	583	589	594	605	619	635	655	675	692	707	715	726	738	760		
45	535	559	581	594	604	610	615	625	640	655	675	695	712	728	737	749	762	785	812	896
45½		580	603	616	626	631	636	646	661	675	695	715	732	749	760	773	786	810	836	918
46		602	626	639	649	653	658	667	682	696	716	736	752	770	783	797	811	836	861	941
46½			649	661	671	676	680	689	704	717	737	756	773	792	806	822	837	862	886	964
47			673	685	695	699	702	712	726	739	758	777	794	814	829	847	863	888	911	987
47½				710	719	723	725	735	749	761	779	799	815	837	853	873	890	915	937	1010
48				735	744	747	749	758	772	783	801	820	837	859	878	899	917	942	964	1034
48½					769	772	773	782	795	806	824	842	859	882	903	926	945	970	991	1058
49					795	797	798	807	819	829	847	865	882	906	929	953	974	999	1018	1082
49½						823	823	832	844	853	870	888	905	930	955	981	1003	1028	1046	1106
50						849	849	858	870	878	894	911	929	955	981	1009	1032	1057	1074	1131
50½							875	884	895	902	918	935	952	980	1008	1038	1062	1087	1103	1156
51							902	910	921	927	943	959	976	1005	1035	1068	1093	1118	1133	1182
51½								937	947	953	967	983	1001	1030	1063	1098	1124	1149	1163	1208
52								964	974	979	992	1008	1026	1056	1091	1128	1156	1181	1193	1234
52½									1002	1005	1018	1033	1051	1083	1120	1159	1188	1213	1224	1260
53									1030	1032	1044	1059	1076	1110	1149	1190	1221	1246	1255	1287
53½										1060	1071	1085	1102	1137	1179	1222	1254	1280	1286	1314
54										1087	1098	1111	1128	1165	1209	1255	1288	1314	1318	1341
54½											1125	1137	1155	1193	1239	1288	1323	1348	1351	1369
55													1182	1221	1270	1322	1358	1383	1384	1397
55½																1356	1394	1418	1418	1425
56																			1452	1453

Chapter 18

Aging in Relation to Growth and Efficiency with Special Reference to Milk and Egg Production*

> Death is the end point in a long chain of events, and biologically it may be best understood in terms of the antecedent physico-chemical processes.
> *A. E. Cohn*

Long life, the resultant of a sound, harmoniously functioning, slowly-aging body, is an obviously important factor in the long-range efficiency complex. Dairy cattle, for example, do not pay for themselves in milk and calves until they are about four years old, and the longer thereafter they maintain a satisfactory yield the greater the clear profit on the growth investment. The same holds true for many other productive processes, including those of man, who often requires 25-odd years of rearing and formal education for productive work and 25 years for proving himself. The phenomenon of aging is, therefore, of great agricultural and social importance as well as of personal and scientific interest.

The age at death is determined by two more or less interrelated sets of causes: (1) *external*, *i.e.*, from infections (scarlet fever, typhoid, tuberculosis, etc.), especially in the young, and (2) *internal*, *i.e.*, from the insidiously developing degenerative diseases (Fig. 18.10, after Pearl[1]).

Many external causes of human death, particularly infections, are being brought under control by public health measures, by more efficient antisepsis, and by better personal hygiene, with the result that the *average* expectancy of life is increasing. Thus while in ancient Rome the average life expectancy at birth was 25 years, in contemporary (pre-war) Rome it is 55 years, and in contemporary continental United States it is about 64 years[2]; and the former major cause of death, infectious diseases such as tuberculosis, is giving place to non-infectious diseases, such as heart disease.[3]

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* Grateful acknowledgements are made to Drs. E. J. Stieglitz, L. K. Frank, C. M. McCay and Ralph Bogart for critical reading of parts of this chapter; also to Dr. C. E. Marshall, Professor of Colloid Chemistry and to Dr. A. E. Stearn, Professor of Physical Chemistry at the University of Missouri.

[1] Pearl, R., and Raenkham, T., *Human Biology*, **4**, 80 (1932).

[2] Rise in the mean life expectancy in the United States: 1800, 36 years; 1850, 40 years; 1900, 50 years; 1920, 55 years; 1930, 60 years; today, 64 years. In the 1920–40 period death rates from tuberculosis and pneumonia approximately halved; from circulatory disease approximately doubled.

[3] Report to the National Resources Committee on The problem of a changing population, Government Printing Bureau, Washington, 1938.

Incidentally, the increase in average life expectancy increases the percentage of persons in the older age groups (Fig. 18.1a). In 1850, half of the population was adult, above 18 years; today about two-thirds of the population is over 18 years.[3] During the brief 1930–40 interval those of 65 years and above increased by 35 per cent, whereas the total population increased by only 7 per cent. The increase in the percentage of older persons, of course, raises interesting problems. Thus wisdom tends to be cumulative, to increase with increasing experience associated with the passing years, and from this viewpoint the longer the survival (prior to senile dementia) the greater the social gain on the initial rearing and education investment. History is replete with epochal contributions of men old in years and wisdom—Goethe, Michelangelo, Benjamin Franklin, Justice Holmes. Unfortunately, not only wisdom and generosity, but also folly, cruelty, maladjustment and invalidism tend to be cumulative. Similar young develop into different old, exerting different influences on society. Moreover, this rate of change differs. Some are mentally, emotionally, and in general physiologically old at 40 years; others are young at 80 years and wiser.

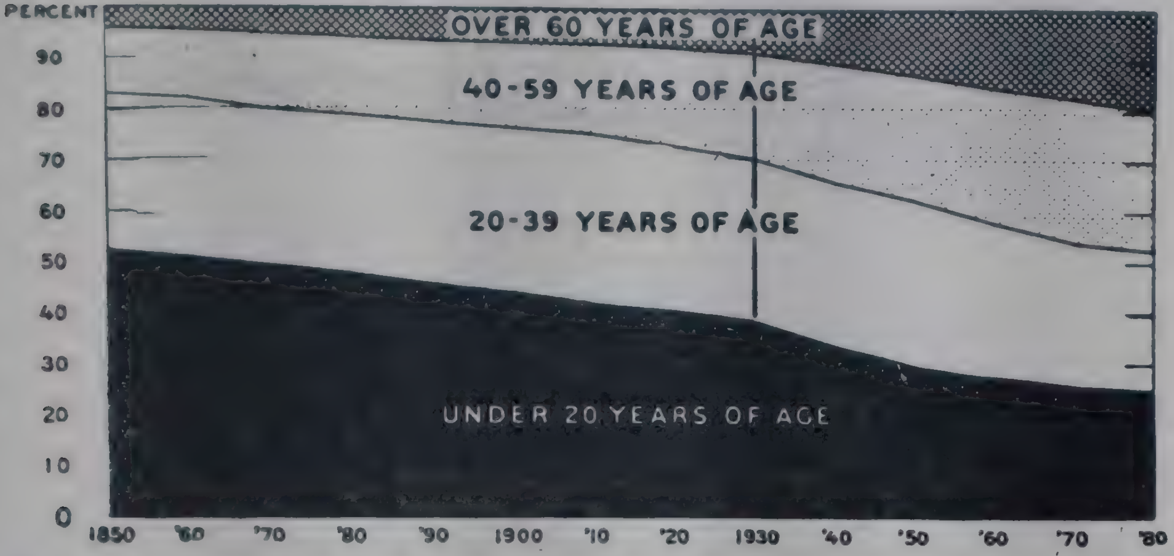

Fig. 18.1a. The influence of control of infectious disease on the age of distribution of the population. (Reproduced from negative 27324-A, Bureau Agricultural Economics, U. S. Dept. Agriculture.) The population under 20 years of age was over 50 per cent in 1870, 40 per cent in 1930, 35 per cent in 1940, and (it is estimated to be) 30 per cent in 1950, 25 per cent in 1980. The population between 20 and 60 years of age was 45 per cent in 1870, 53 per cent in 1930, and (it is estimated to be) 57 per cent in 1950, and 55 per cent in 1980. The chart was prepared from the following data (Report to the National Resources Committee, Government Printing Office, 1938):

Population, Per cent

Year	Under 5 yrs. of age	5–19 yrs.	20–44 yrs.	45–64 yrs.	Over 65 yrs.
1850	15.1	37.4	35.1	9.8	2.6
60	15.4	35.8	35.7	10.4	2.7
70	14.3	35.4	35.4	11.9	3.0
80	13.8	34.3	35.9	12.6	3.4
90	12.2	33.9	36.9	13.1	3.9
1900	12.1	32.3	37.8	13.7	4.1
10	11.6	30.4	39.1	14.6	4.3
20	11.0	29.8	38.4	16.1	4.7
30	9.3	29.5	38.3	17.5	5.4
35	8.5	28.2	38.6	18.8	5.9
40	8.3	26.4	38.8	20.2	6.3
50	7.9	23.1	39.7	21.4	7.9
60	7.1	22.2	37.4	23.3	10.0
70	6.7	20.6	35.0	25.9	11.8
80	6.4	19.6	33.7	25.9	14.4

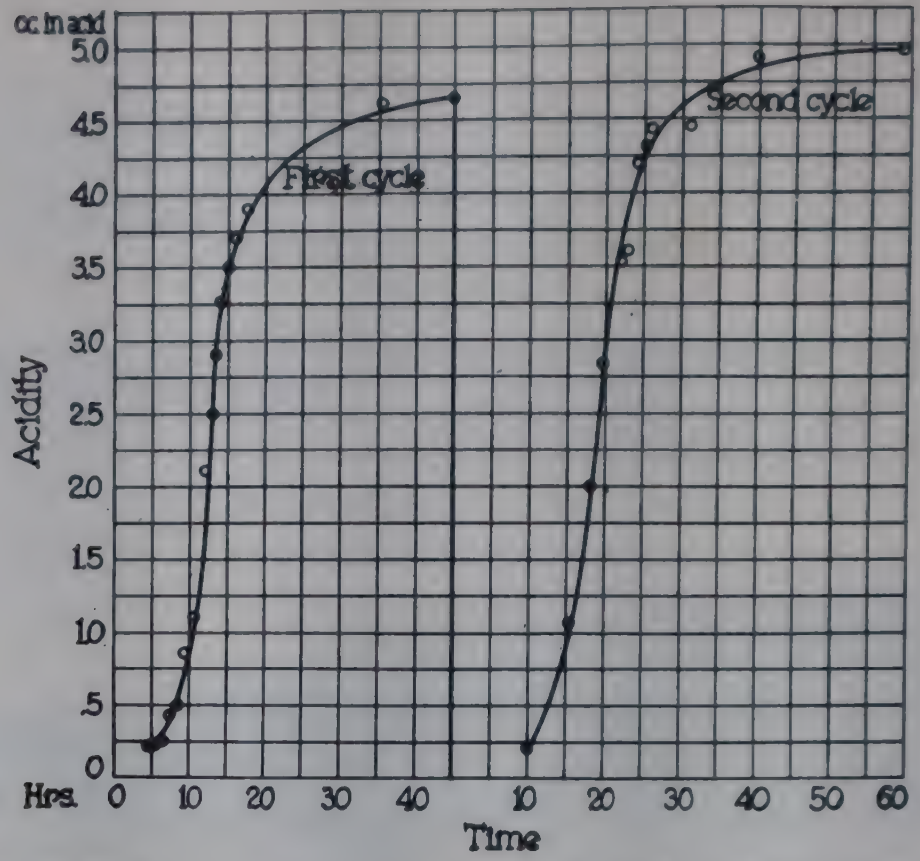

Fig. 18.1b. The first cycle represents the course of growth and senescence of a culture of lactic-acid producing bacteria in milk. Growth ceases after a characteristic concentration of lactic acid is attained. The proof that the accumulating acid is the limiting factor in growth is furnished by the fact that when the sour milk was neutralized with lime water, a second growth cycle was produced, virtually a duplicate of the first cycle. Similar curves result when food is a limiting factor. Cessation of growth leads to death of the bacteria.

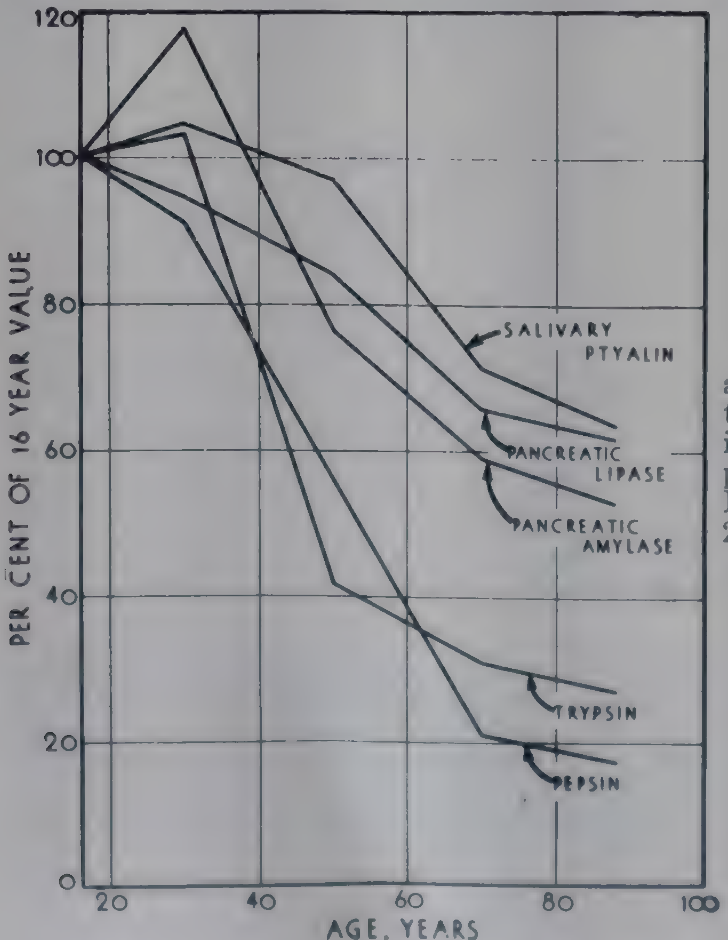

Fig. 18.2. Age course of enzymatic activity in the human alimentary tract. Interpolated and recomputed in terms of percentage values and plotted from charts by Meyer, J., and Necheles, H., *J. Am. Med. Assn.*, **115**, 2050 (1940).

Returning to the causes of death, the controllable external causes of the chance variety need no explanation except insofar as accidents are more likely to be fatal to the old because of reduced reserve power. Indeed, decline in the reserve power, or in the safety factors, required to withstand the stresses and strains of life is the best index of the aging process, and a theory of senescence should explain this decline.

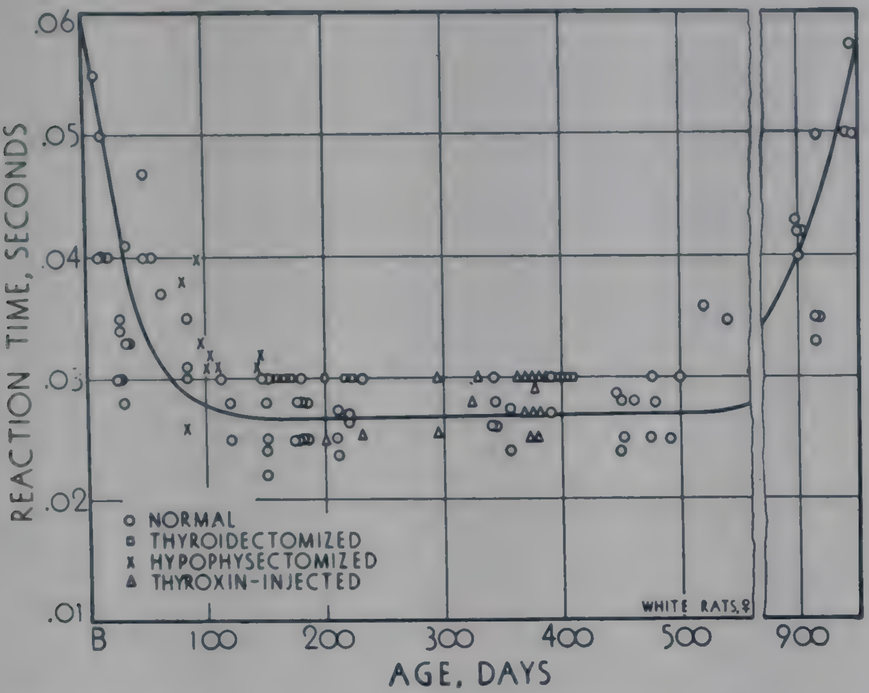

Fig. 18.3a. Age course of reaction time to a simple electric shock in rats. From E. B. Brody, *J. Gen. Physiol.*, March 15 (1941). Note how the infantile reaction time recurs during senescence, but, of course, actuated by different factors.

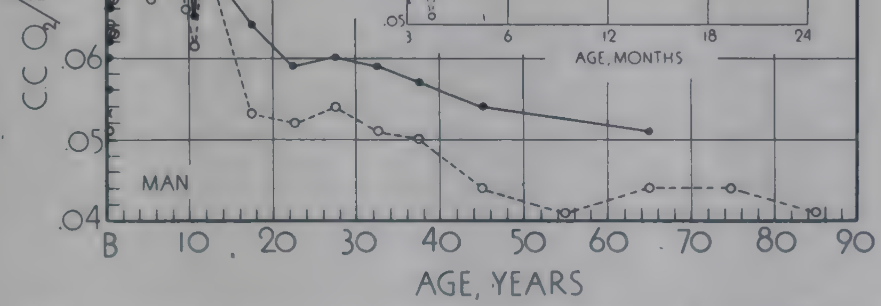

Fig. 18.3b. Age changes in the cardio-respiratory reserve of man. Unpublished chart by H. H. Kibler, prepared from the numerous published papers by F. G. Benedict and associates.

The outstanding surveys of published literature[4] and of projected studies[5] on aging do not offer a general theory. Some maintain that aging is a cumulative expression of repeated environmental insults (infections, improper diet, toxic substances in the atmosphere, worry, etc.) which initiate and accelerate irreversible changes constituting senescence. It is agreed that external

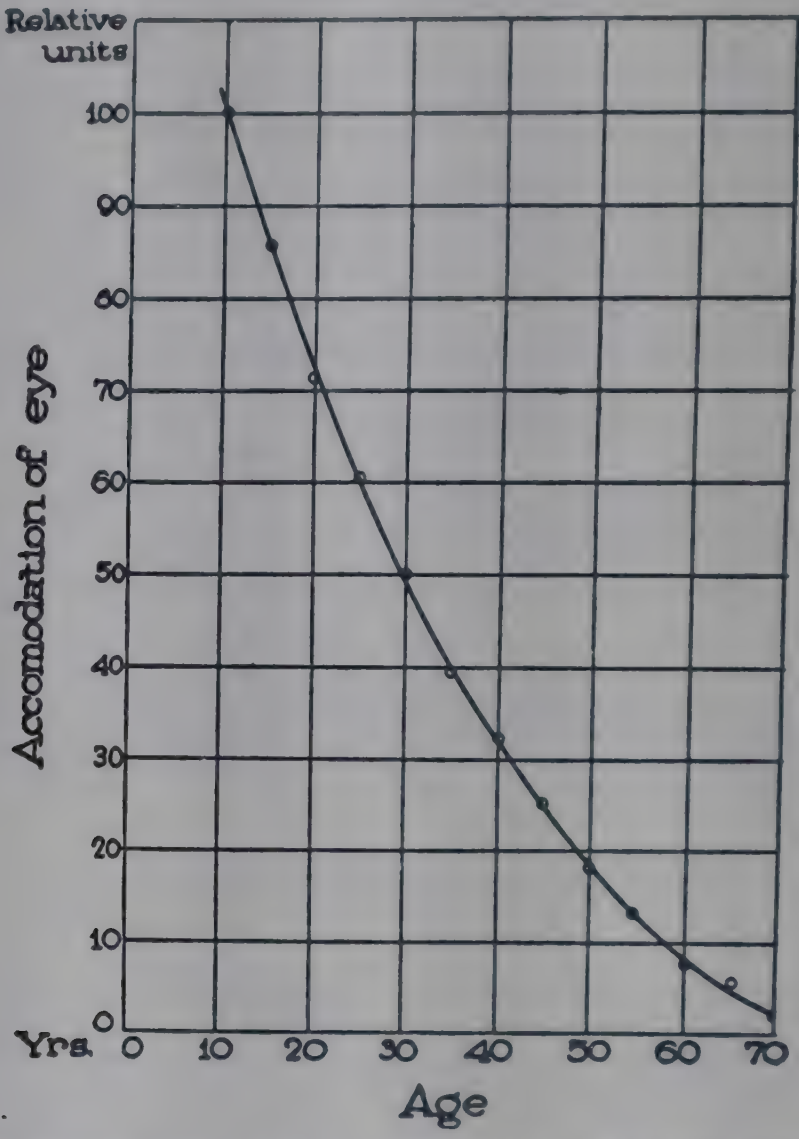

Fig. 18.4. Decline in the range of accommodation of the eye (presbyopia). "The change is due to the hardening of the lens by loss of water and the deposition of cholesterol and some insoluble globulins. . . . The early presbyopes die early, the late presbyopes die late."—Felix Bernstein, *Symposia on quantitative biology*, **2,** 214 (1934). "The lens grows throughout life . . . the lens contains from birth to old age . . . embryonal parts . . . difference in relative proportion of young and old tissue within it." J. S. Friedenwald, *in:* "Problems of Ageing," p. 512.

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[4] Cowdry, E. V., Editor, "Problems of Ageing", Baltimore, 1939. Foreword by L. K. Frank, introduction by John Dewey, and 25 chapters by 25 authors on subjects ranging from aging of plants to aging of psychological processes. Steiglitz, *J. A. M. A.*, **116,** 1183 (1941), and News Edition, *Am. Chem. Soc.*, **19,** 1147 (1941); *Sci. Monthly*, June (1944); "Geriatric Medicine", Saunders, 1943, Korenchevsky, V., "The war and the problem of ageing", *Jour. Am. Med. Assoc.*, **119,** 624 (1942). MacNider, Wm. de B., *Science*, **99** (1944).

[5] Stieglitz, E. J., Report of a Survey of Active Studies in Gerontology, National Institute of Health, U. S. Public Health Service, 1942.

causes condition the *average* expectancy of life at birth, but it is not agreed that such external causes condition the *individual* maximum life span. The life span of *Drosophila* was not increased, indeed it was reduced somewhat, by aseptic housing.[6] Just as the maximum life span of man is about 100 years, so of *Drosophila* it is about 100 days and of the white rat about 1000 days. Each apparently grows and ages by its own hereditary clock (Ch. 19).

Senescence and death are, of course, not inherent in unicellular organisms, such as bacteria or yeasts; they simply divide continuously, provided, however, that the metabolic products (as lactic acid, illustrated by Fig. 18.1b, or alcohol) are removed from and food supplied to the culture medium.[7] But if growth stops, due either to accummulation of metabolic products or exhaustion of food, senescence processes set in and death follows.[8]

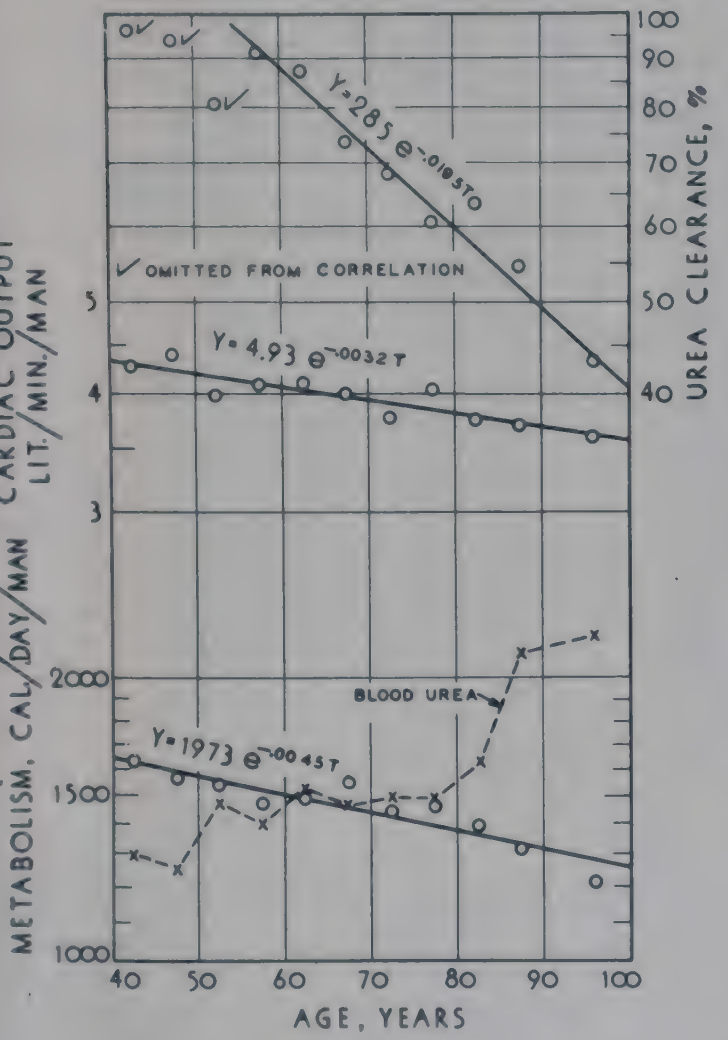

Fig. 18.5. Age curves of basal metabolism, cardiac output, urea clearance, and blood urea concentration. Recomputed, equations fitted, and plotted from: *basal metabolism*, W. H. Lewis Jr., *Am. J. Physiol.*, **121,** 502 (1938); *cardiac output*, W. H. Lewis, Jr. *Id.*, p. 517; urea clearance (ability of kidney to remove urea from blood), and *blood urea concentration*, W. H. Lewis, Jr., and A. S. Alving, *Id.*, **123,** 500 (1938). As before, the exponents in the equations multiplied by 100 represent instantaneous percentage decline per year. These equations were fitted to the data by the method of least squares.

Likewise, many tissues from higher organisms are potentially immortal, as demonstrated by the continuous growth of cancer tissue[9] when transplanted to successive animal generations and by continuous growth of normal tissues when transplanted at sufficiently frequent intervals into fresh culture media.[10] One of the tissue cultures obtained by Carrel from the chick heart

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[6] Loeb, J., *Sci. Monthly*, **9,** 580 (1919). Bogdanow, E. A., *Arch. ges. Physiol.*, (1906), and *Arch. Anat. and Physiol.*, (1908).

[7] *Cf.* Woodruff, L. L., "A long-continued pedigree culture of *paramecium*". *Proc. Nat. Acad. Sci.*, **7,** 41 (1921).

[8] Falk, I. S., and Winslow, C-E. A., *J. Bact.*, **11**, 1 (1926). Rahn, O., "Physiology of bacteria", Philadelphia, 1932.

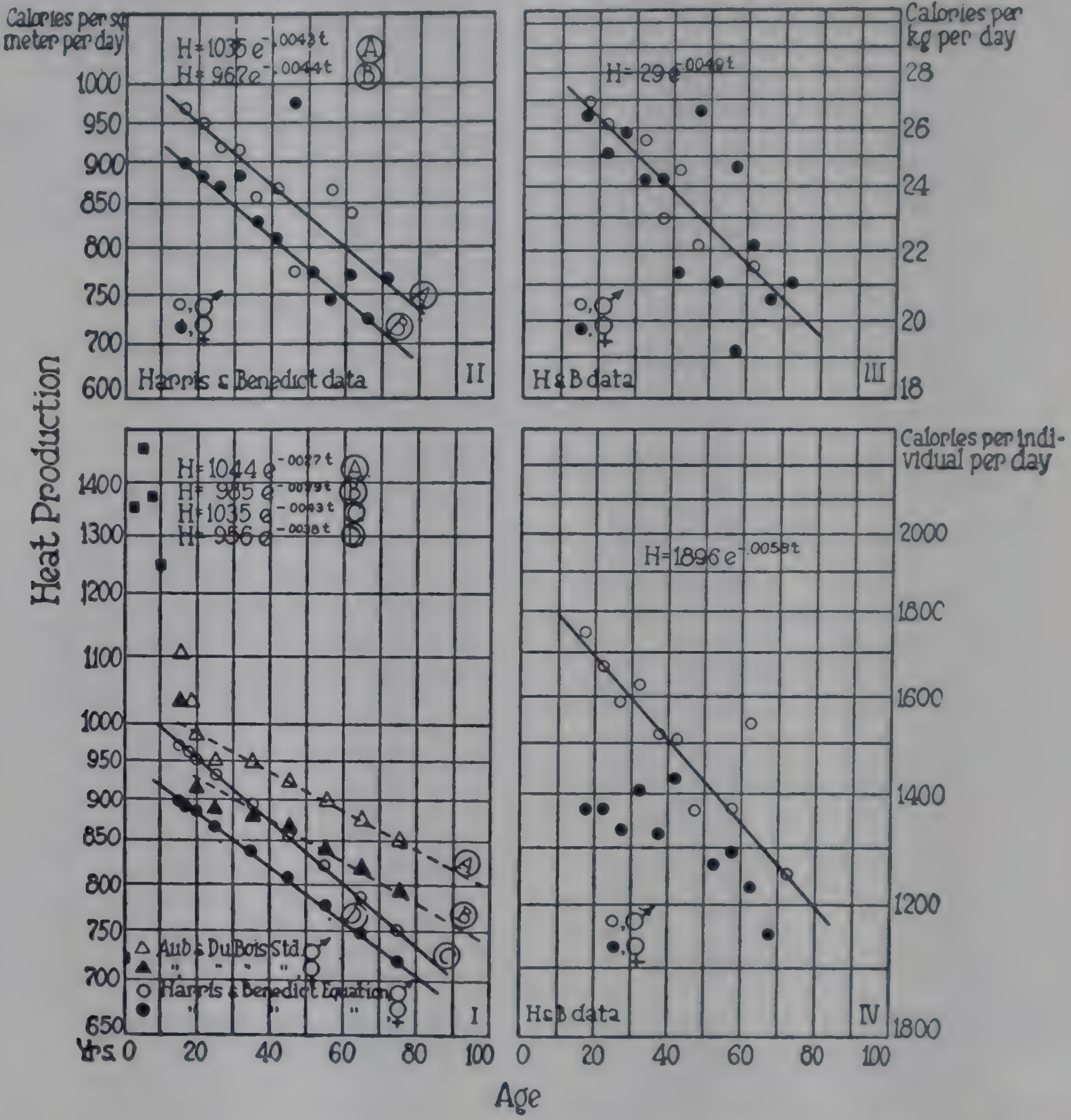

Fig. 18.6. Age curves of basal heat production plotted on arithlog grids. Quadrants, II, III, and IV represent the daily metabolism, respectively, per unit surface area, per unit weight, and per individual, all plotted from data by Harris and Benedict, Carnegie Inst. of Washington, Pub. 279, pp. 123 and 118. Our numerical values of the exponents indicate that the metabolism declines at the approximate rate of 0.5 per cent per year; the exact value depends on the reference bases. We assume that the metabolism curves are exponential, declining at a constant *percentage* rate; Harris and Benedict assumed that the metabolism curves are linear, declining at a constant *absolute* rate (decline by 7.15 Cal. per year for men and 2.29 Cal. per year for women). Quadrant I represents the metabolism "standards" of Harris and Benedict, and of Aub and Du Bois to which we fitted equations. (See E. F. Du Bois' book "Basal Metabolism in Health and Disease".)

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[9] Loeb, Leo, "On transplantation of tumors", *J. Med. Res.*, **6,** 28 (1901). "Tissue growth and tumor growth", *J. Cancer Res.*, **2,** 135 (1917). "Transplantation and potential immortality of mammalian tissues," *J. Gen. Physiol.*, **8,** 417 (1926).

[10] Carrel, Alexis, "On the permanent life of tissues outside of the organism," *J. Exp. Med.*, **15,** 516 (1912); "Measurement of the inherent growth energy of tissues."*Id.*, **38,** 521 (1923). Carrel and Ebeling, A. H., "The multiplication of fibroblasts *in vitro*," *Id.*, **34,** 317 (1921), and many subsequent papers.

in January, 1912, is still growing by the continuous-transplantation method, thus demonstrating that body cells are also potentially immortal. But in the

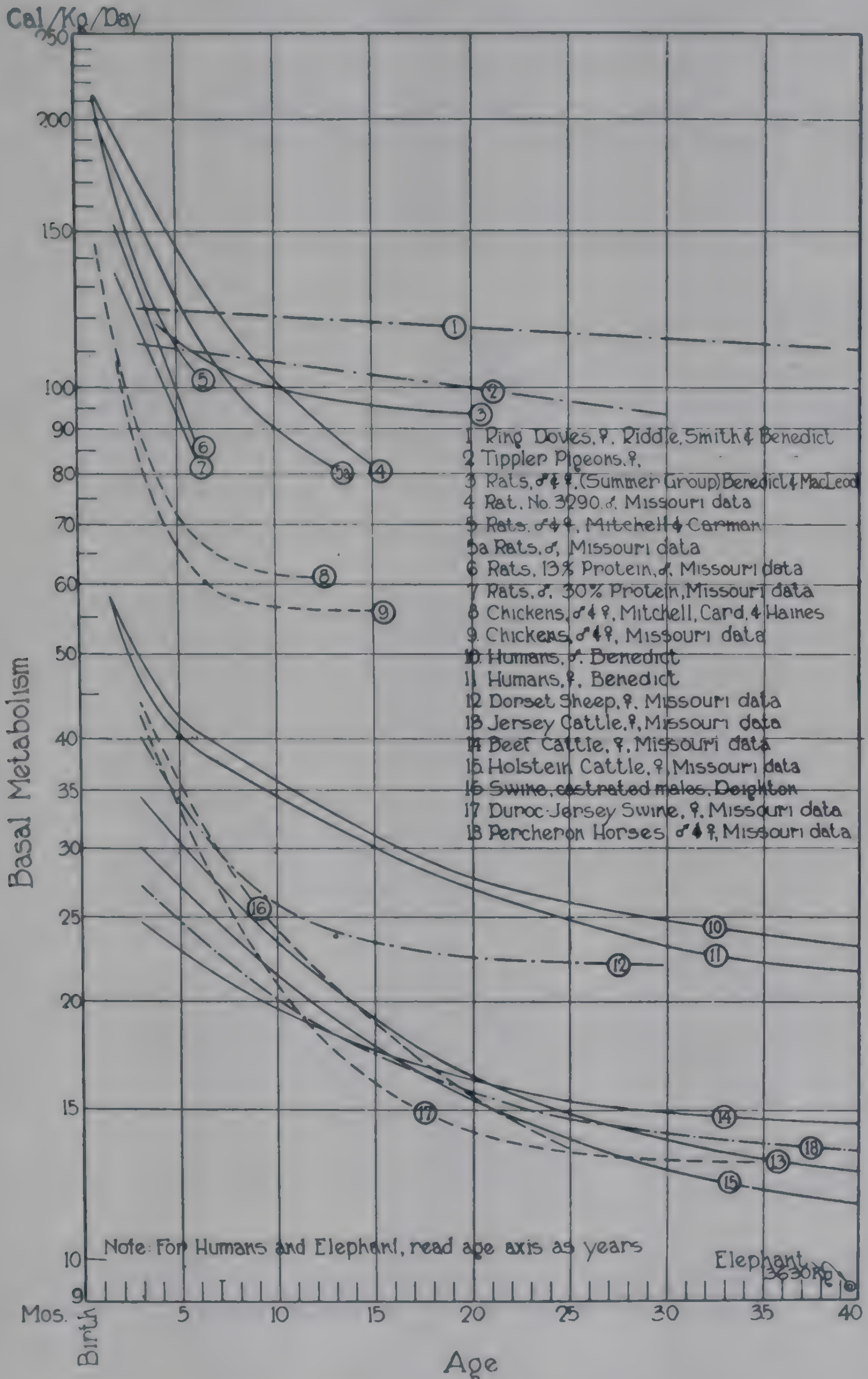

Fig. 18.7. Age course of metabolism per unit weight plotted on arithlog paper. Ages are in months, except for humans and elephants in years. The numbers on the curves refer to corresponding legends on the chart. The elephant, like the horse, was measured in a standing position. See Missouri Agr. Exp. Sta. Res. Bull., 176, 1932, for details about the data.

body, as part of a closed system, they age and die. How shall one explain the mortal nature of the closed system in the face of the immortality of the component cells?

Many years ago Minot[11] wrote dramatically on the meaning of senescence: that the percentage growth rate declines with age and that "retardation of growth is old age and its cessation is death". According to this theory, generally accepted in principle, the aging process begins with the onset of life and is, indeed, most rapid at the earliest ages. Pragmatically, however, the aging of a given function is said to begin when the peak is passed. Thus a prize fighter is said to be old at 30 because his fighting ability has passed its peak, and is on the decline; a Supreme Court justice may be young at 70 years because his judicial wisdom may then still be at its peak.

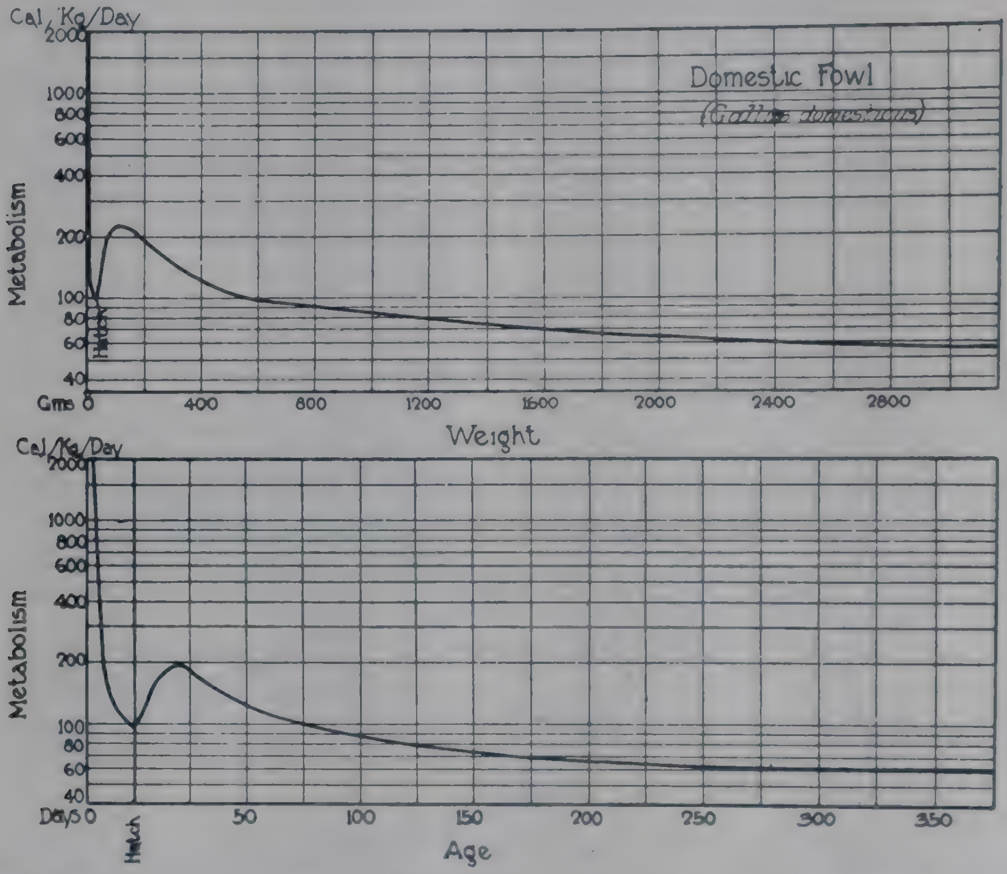

Fig. 18.8. The age course of metabolism per unit weight of the domestic fowl. For details see Missouri Agr. Exp. Sta. Res. Bull., 176.

18.1: Physicochemical theory of aging. But why does cessation of growth lead to death? The simplest explanation is that body colloids, such as tissues, undergo progressive aging in the manner of non-living colloids.[12] Bancroft's[13] suggestion that sodium rhodanate (NaCNS?) when taken "about a teaspoonful a week of a 10% solution" may "retard the aging of the colloids of the body" calls attention, in a highly over-simplified manner, to the colloidal theory of senescence. Many age changes in the body are such as might be expected from the assumption that its colloids are setting. Thus progressive dehydration[14] with consequent decrease in the degree of dispersion and in related physicochemical changes[12] in the tissues are similar to those occurring in other non-living colloids. Reduction in elasticity,[15] surface energy, and chemical reactivity are equally marked in aging inorganic and in body colloids. The rates of virtually all metabolic processes (Figs. 18.1 to 18.8) decline with increasing age, as might be expected from progressive decline in physicochemical reactivity. The age curve of ionic interchange is in harmony with the colloidal aging theory.[16] The aging of tissues is apparently

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[11] Minot, C. S., "Senescence and rejuvenation," *J. Physiol.*, **12**, 97 (1889). "The problem of age, growth, and death," New York, 1908.

[12] Dhar, H. R., "Old age and death from a chemical point of view," *J. Physical Chem.*, **30**, 378 (1926), and **34**, 549 (1930).

[13] Bancroft, W. D., *et al.*, *Science*, **80**, 549 (1934), and **81**, 152 (1935).

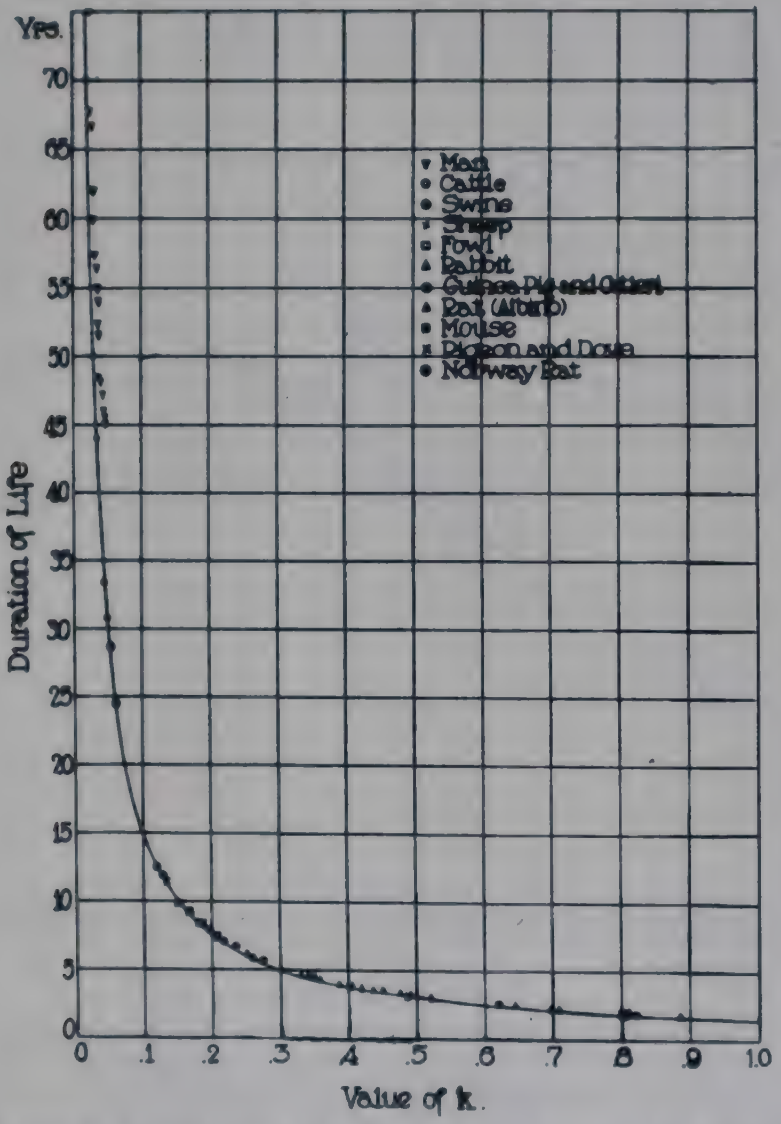

Fig. 18.9. Estimated duration of life of different species as function of the rate, k, of approach to mature weight. The longer the growth period (the smaller the value of k), usually the longer the life span.

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[14] Moulton, C. R., *J. Biol. Chem.*, **57,** 79 (1923). McCay, C. M., in Cowdry, E. V.,[4] pp. 592–617. Murray, H. A., Jr., *J. Gen. Physiol.*, **9,** 789 (1926). Murray, J. A., *J. Agr. Sci.*, **12,** 103 (1922). H. S. Simms and A. Stolman, *Science*, **86,** 269 (1937), reported that tissue from persons over 70 years contained more water, chloride, total base, sodium, and calcium and less potassium, magnesium, and ash than from persons 30 to 40 years old.

[15] Steele, J. M., "Changes in elasticity with age," *Abst. Div. Biol. Chem. Am. Chem. Soc.*, Sept. 8, p. 2B (1941).

[16] Jenny, H., *J. Physical Chem.*, **40,** 501 (1936).

accelerated by increasing temperature [17] in the same manner as the aging of inorganic colloids.

Dhar[12] suggested that death "from old age" in homeotherms occurs when the oxidation or metabolic rate falls below a certain level required for homeothermy. Figs. 18.5 to 18.8 (and data on pp. 707–9) on the decline in metabolic rate with increasing age may be illustrated by the following numerical data, obtained nearly a half century ago by Magnus-Levy[18] on the metabolism of different individuals at different ages but of the same size.

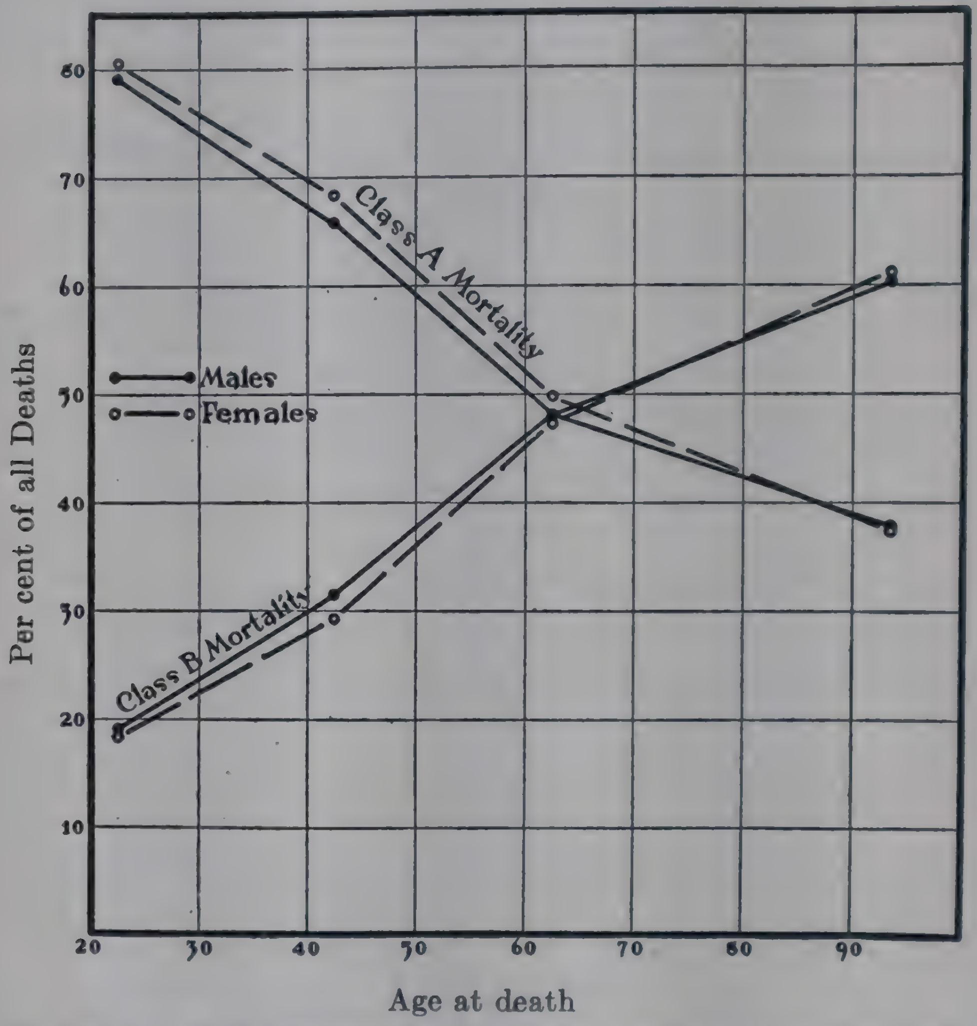

Fig. 18.10. Age trends in percentage mortality due to breaking down of (A) organ systems normally in direct contact with the external environment (plus external causes except suicide); and (B) organ systems normally not in direct contact with the external environment (plus "senility"). Chart by Pearl, R., and Raenkham, T., "Constitutional factors in mortality at advanced ages." *Human Biology*, **4**, 115, (1932).

Age	Body weight (kg)	Metabolism (O_2/min.)
15	44	217
24	43	196
71	48	163

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[17] See Chapter 11, and Loeb, J., and Northrop, J. H., *Proc. Nat. Acad. Sci.*, **2**, 456, (1916), and **3**, 382 (1917); also *J. Biol. Chem.*, **32**, 103 (1917).

[18] Magnus-Levy, A., and Falk, E., *Arch. f. Anat. u. Physiol. Suppl. Bd.*, 315 (1899).

The latest contribution to the problem on the interrelation of metabolism and age is also by Magnus-Levy,[19] made a half century after the first report. The decline in total metabolism with increasing age is associated in part with declining body weight and in part with advancing age, as indicated by the decline in metabolism per unit area. The decline is small, but it does not take much of a metabolic decline to reduce the body temperature to an unsafe level in the old when the homeothermic reserves are at a low level.

Data on the metabolism of aging rats[20] likewise indicate a slight decline in metabolism with increasing age. It was previously noted (Ch. 6) that many disabilities associated with aging may be viewed as being due in large measure to declining ability of the circulatory system to supply oxygen to the tissues and of the declining ability of the tissues to utilize the oxygen. But what causes these declines? Perhaps the setting of the colloids of the circulatory system and of the tissues in general.

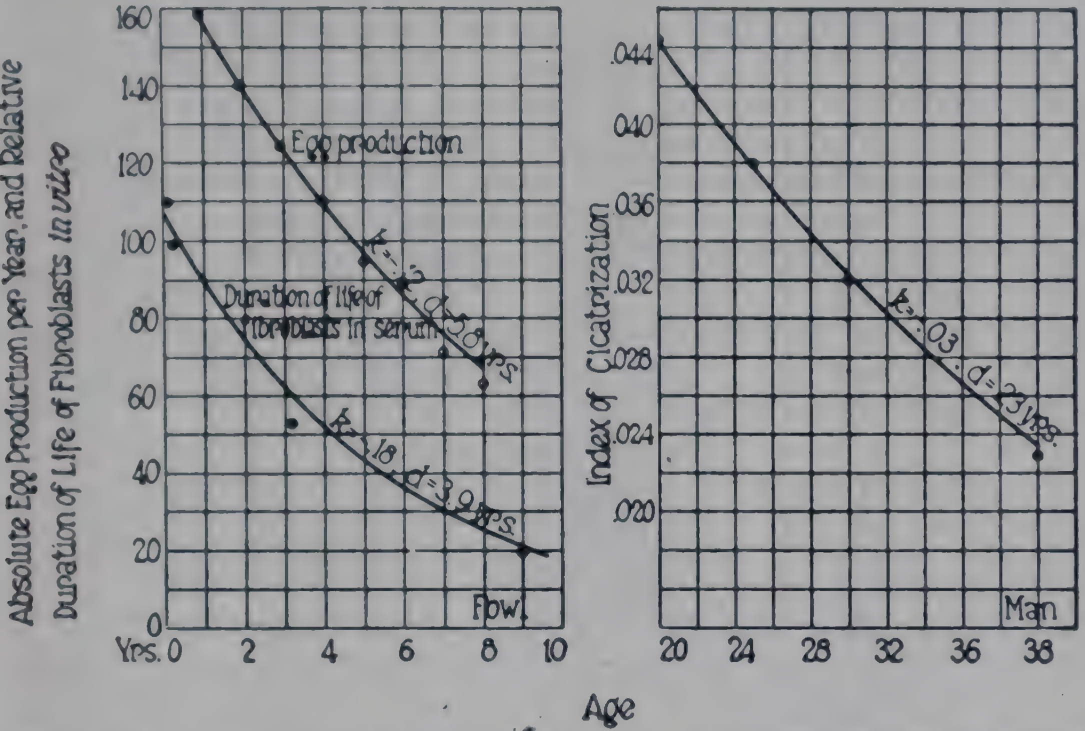

Fig. 18.11. The age course of senescence in man as measured by the time rate of healing of wounds at different ages, and in domestic fowls by the time rate of egg production, and by the duration of life in fibroblasts grown in blood serum of chickens of different ages. 100 k represents the percentage decline for the unit of time indicated on the age axis. d represents the time required for any value to decrease to half, thus the time rate of egg production is halved in 5.8 years.

Senescence has been attributed to the declining functions of some limiting endocrine glands, such as the thyroid, adrenal, and gonad. The gonads are not in the class of senescence-limiting, since castrated animals live as long, probably longer, than normal. The thyroid, adrenal, and other glands may become relatively overactive as well as underactive with increasing age—a problem for medical treatment[21]. The colloidal-energetic theory of senescence offers the simplest and most reasonable explanation of many phenomena.

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[19] Magnus-Levy, Adolph, "Basal metabolism in the same person after an interval of fifty years," *Jour. Am. Med. Assoc.*, **118,** 1369 (1942).

[20] Benedict, F. G., and Sherman, H. C., *J. Nut.*, **14,** 179 (1937). Davis, J. E., *Ann. J. Physiol.*, **119,** 28 (1937). Belasco, I. J., and Murlin, J. R., *Endocrinology*, **28,** 145 (1941). Brody, S., and Windes, A. C., unpublished data.

[21] See, for example, Loehner, C. A., "Effect of adrenal cortex extract on psychotic patients," *Endocrinology*, **23,** 507 (1938), and **27,** 378 (1940).

18.2 : Control of aging. In farm animals in particular and herbivorous animals in general deterioration of teeth is often the limiting factor which leads to digestive disturbances, malnutrition and ultimately death. In other species, particularly in humans and in working animals, deterioration of the cardiovascular renal system is often the limiting factor and cause of death (Fig. 18.10). The adequacy of the internal environment is dependent on that of the cardiovascular-renal system.[22] In the words of Pearl,[1] "if the upper limit of the human life span (as distinguished from the average duration of life) is to be materially extended beyond what it now is, it will be necessary

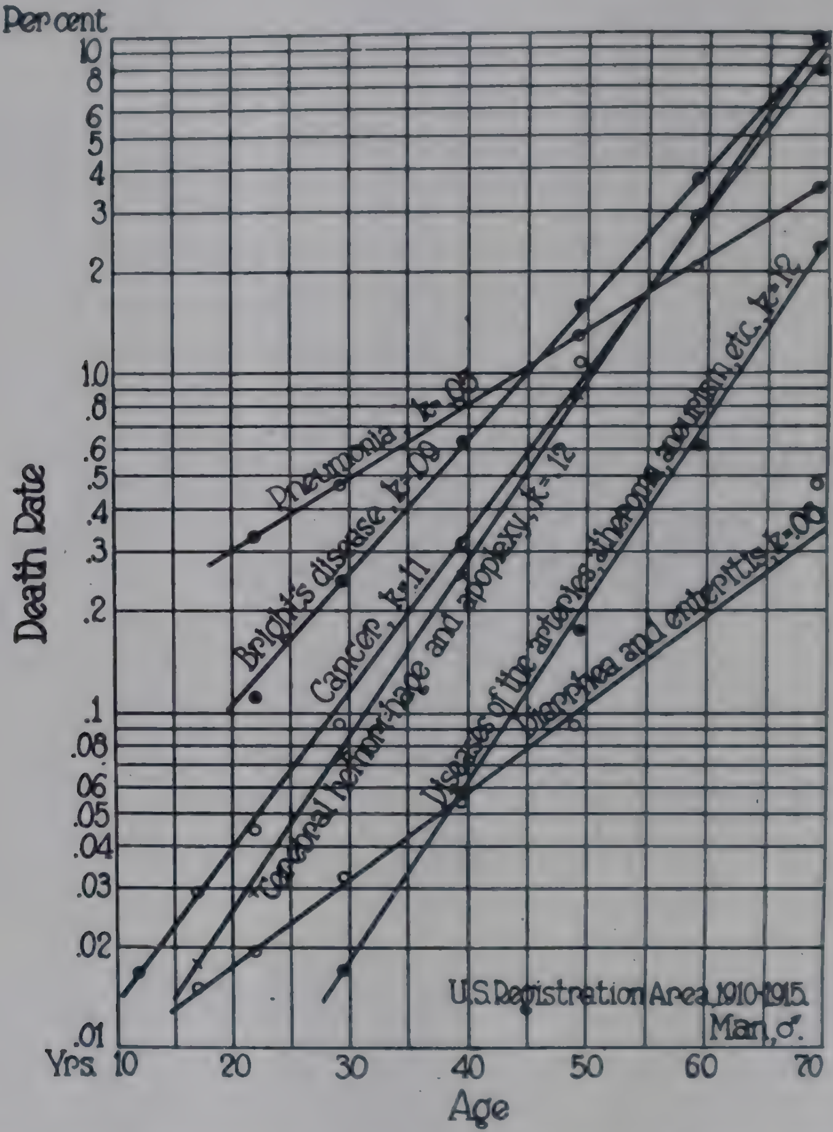

Fig. 18.12. The specific mortality of the given population of man appears to increase with increasing age of the surviving population. Thus the percentage mortality due to pneumonia increases at the rate of 5 per cent per year; or the mortality is doubled in 13.9 years (d represents the time in years in which the mortality is doubled). The increases in percentage mortality due to different causes are different; but for all the given causes the increases take place at a constant percentage rate as indicated by the linear distribution of the data on the arithlog grid.

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[22] Cf. Carlson, A. J., "An unwritten chapter in the physiology of aging," *Sci. Monthly*, July 1939.

for man to acquire, by some means not yet clear, a circulatory system organically superior to the already extremely good one—taken at its best—that he now has". The second most serious cause of death with increasing

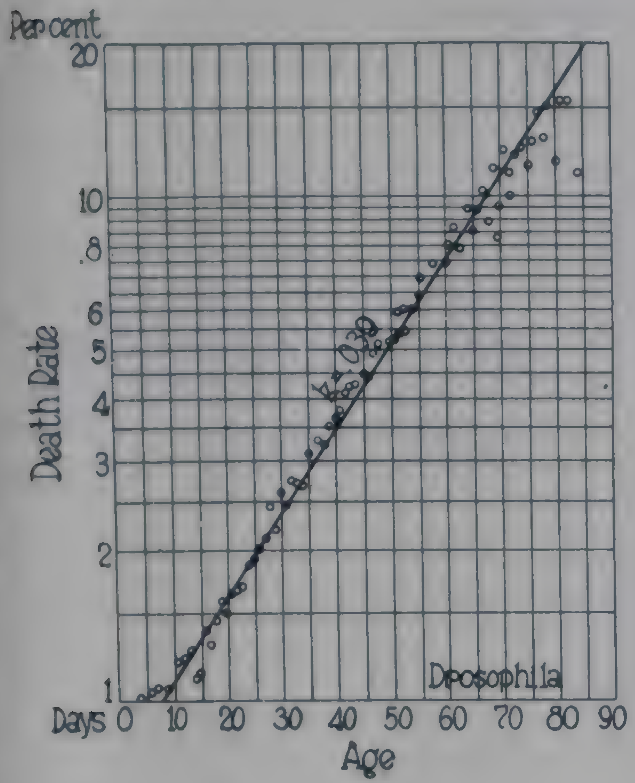

Fig. 18.13. The age course of specific mortality in a population of *Drosophila*. The specific mortality increases at an approximately constant percentage rate, namely 3.9 per cent per day. (The specific mortality is doubled in 17.8 days.)

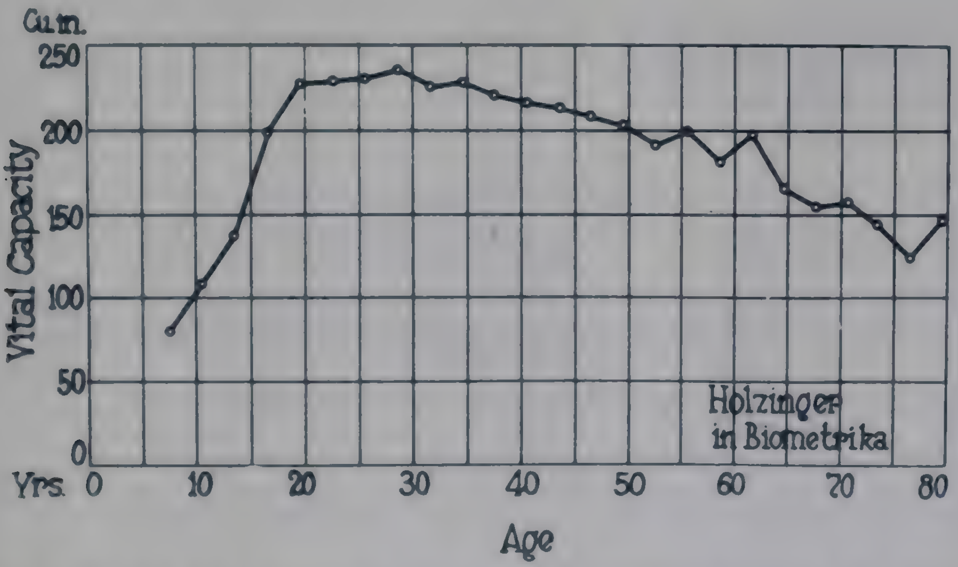

Fig. 18.14. The rise and decline of vital (lung) capacity plotted on arithlog paper. Between 28 and 65 years the vital capacity appears to decrease at the rate of 0.7 per cent per year (a slightly greater value than that for the percentage decline of basal metabolism). If the line is drawn to include age 80 years, the decline is about 1 per cent per year.

age is deterioration of the organismic controls[22a] as manifested by the overgrowth of certain cells leading to cancer.

The simplest way for increasing the longevity of farm animals is by selective mating of the long-lived individuals. The progeny of old parents should

[22a] Little, C. C., *Jour. Am. Med. Assoc.*, **125**, 93 (1944).

tend to be long-lived, and also hardy, because long survival normally reflects a hardy, harmoniously functioning constitution.[23] From the viewpoint of longevity and long-range efficiency the present tendency to overwork and to dispose of animals at early ages is thus unfortunate.

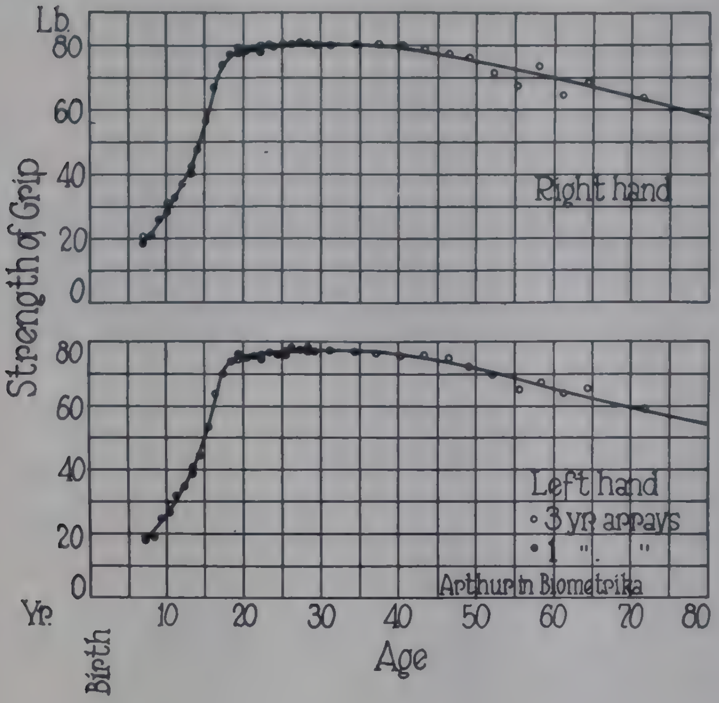

Fig. 18.15. The rise and decline of strength of grip with increasing age. The nature of the distribution of the data does not permit an evaluation of its constants from the present point of view.

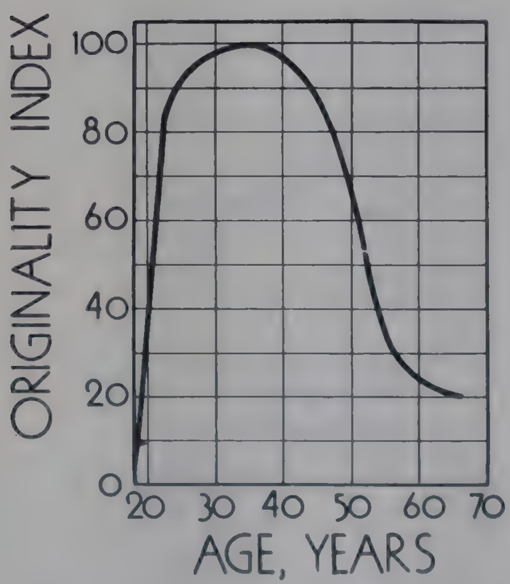

Fig. 18.15a. "Originality" (number of inventions or discoveries) as function of age. From Thomas Midgley, Jr., presidential address, American Chemical Society, Sept. 1944, in Chem. and Eng. News, *Am. Chem. Soc.*, **22,** 1647 (1944). See also Lehman.[60]

The question under consideration, however, is not to develop hereditary long-lived animals, but to control the rate of aging of existing animals. What are the non-genetic factors conditioning longevity?

If one accepts the colloidal theory of aging, control would consist in the first place of making sure of sound development of the tissues by proper nutrition and by avoiding injuries, such as rheumatic fever; and secondly of avoiding influences which tend to "set" the body colloids prematurely. In brief, "the art of prolonging life is not shortening it" (Max Rubner).

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[23] Pearl, R., "Duration of life as an index of constitutional fitness," *Poultry Sci.*, **3,** 1 (1923).

According to the colloidal theory of aging, any factor which accelerates the metabolic processes beyond a relatively low level should accelerate the rate of aging and shorten the life span. The causative factors may be as diverse as muscular work, overactive nervous or endocrine systems, environmental temperature (low for warm-blooded animals, high for cold-blooded), small body size associated with early maturation and high heat production per unit weight, excessively high nutritive level, and so on. The higher mean life span of many female homeotherms may be associated with their lower energy metabolism.[24] Rubner's energetic theory of longevity[25] thus becomes a corollary of the colloidal theory. The influence of metabolic rate on the aging rate and on life span should be somewhat similar to the influence of temperature on the aging rate of inorganic colloids.

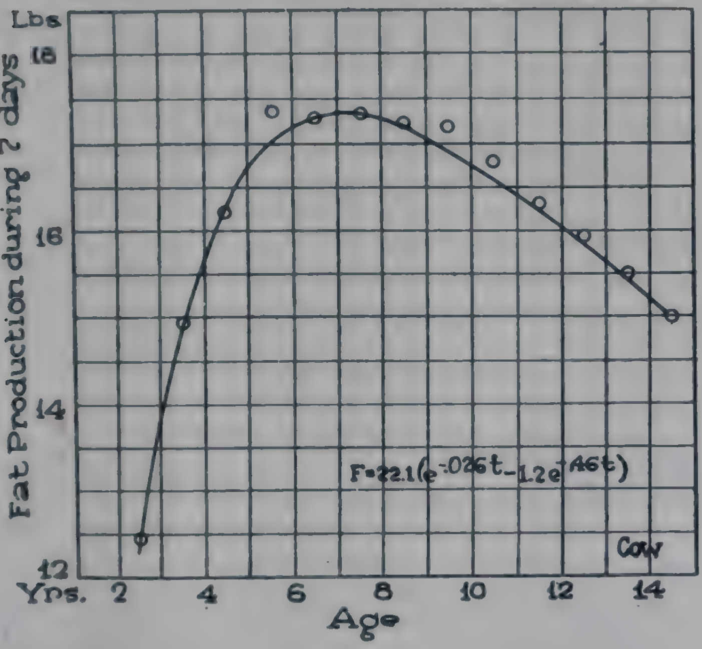

Fig. 18.16. The rise and decline of milk yield with increasing age as indicated by 7-day records from the Advanced Register of Holstein cows. The circles are observed values; the smooth curve represents the equation in the chart. The fit of the equation to the rising segment of the age curve of milk yield indicates that until the maximum, the milk yield follows the course represented by the growth equation 16.12.

Rubner has calculated[25] that the quantity of energy metabolized per kilogram body from maturity to death is nearly the same in warm-blooded animals, except man. This is illustrated by the following estimates:

Species	Body weight (kg.)	Length of life (years)	Calories expended during life time per kilo adult body weight
Horse	450	30	170,000
Cow	450	26	141,000
Dog	22	9	164,000
Cat	3	8	224,000
Guinea pig	0.6	6	266,000

Unlike the above species, which generate about 200,000 Calories per kilo during the life cycle, man was estimated to generate about 800,000 Calories per kilo. This may be correlated with the relatively long growing period,[26] that is, with the delay in the cessation of growth, in man as illustrated in Fig. 16.7, also Figs. 19.4–19.6. It is obvious from the colloidal theory of growth that the longer the delay in growth cessation the longer the maintenance of the freshness of the colloids. The mean persistence of a given tissue is cor-

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[24] Landauer, W., and A. B., *Am. Naturalist*, **65**, 492 (1931).

[25] Rubner, M., "Das Problem der Lebensdauer und seine Beziehungen zum Wachstum und Ernährung," Berlin, 1908.

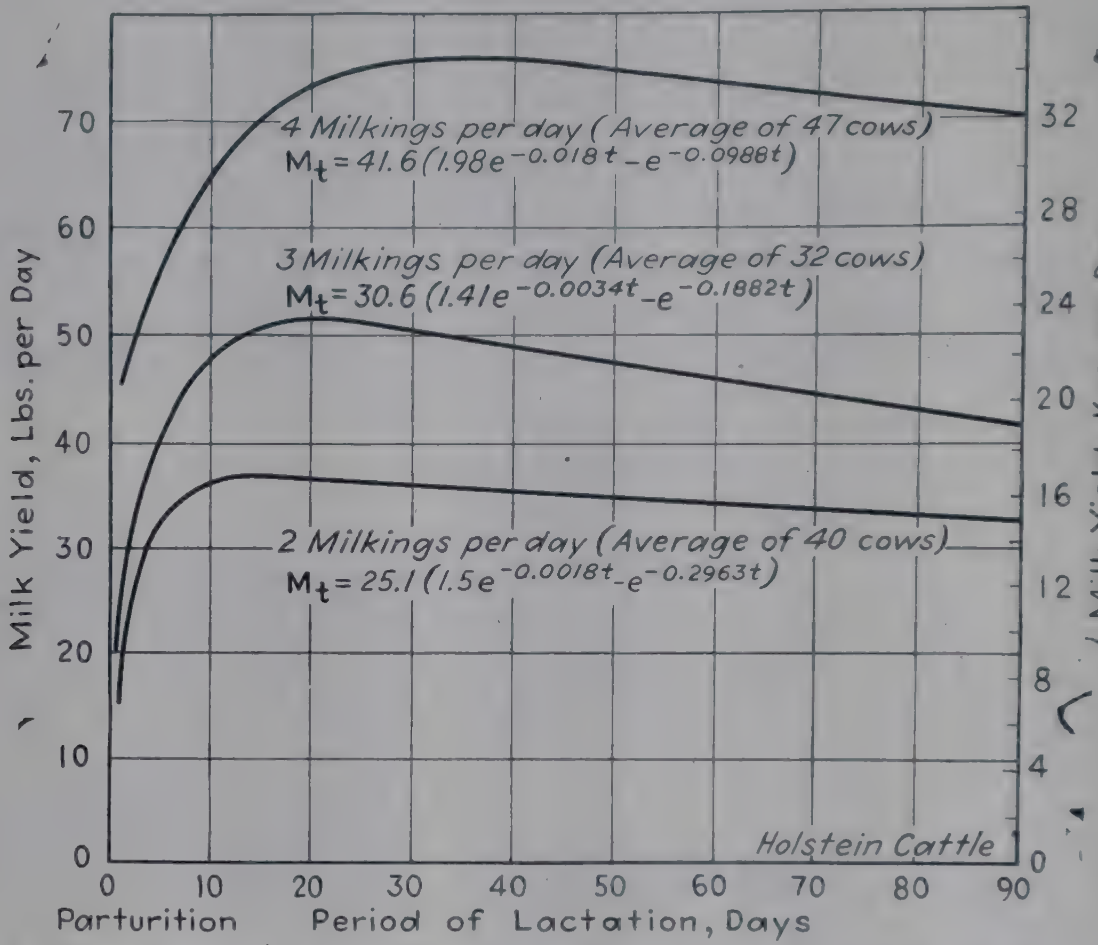

Fig. 18.17. The rise and decline in milk secretion with the advance of the period of lactation of three groups of Holstein cows. The upper curve represents average milk yields of 47 cows milked 4 times a day. The middle curve represents the average yields of 32 cows milked 3 times a day. The lower curve represents 40 cows milked two times a day. The data were compiled by C. W. Turner of this (Dairy) Department (cf. Turner et al., *J. Dairy Sci.*, **6,** 527(1923).

The rising segments are represented by the equation

$$W = A - Be^{-kt} \tag{1}$$

The declining segments by

$$W = Ce^{-k_2 t} \tag{2}$$

W represents milk yield at time t after calving. A is the maximum milk yield. C is the theoretical yield at parturition obtained by extrapolating the declining segment to zero time. k, is the (daily) fractional decline in the successive increases of milk yield for the rising segment. k_2 is the fractional decline in the time rate of milk secretion for the declining segments of the curves. The smooth curves represent a combination of equations (1) and (2), namely

$$W = Ce^{-k_2 t} - De^{-k_3 t} \tag{3}$$

The numerical values of C and k_2 are the same as in equation (2). k_3 is very roughly the difference between k_2 and k, D is not far from the value of B. See Fig. 18.25.

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[26] Lusk, G., "The Science of Nutrition," p. 571–2, 1928 ed.

related with its continuous renewal, its colloidal freshness. Survival is indeed, as Minot expressed it, dependent on continuance of growth. This would be expected to hold for animals of different species, as shown in Fig. 18.9, which indicates that the life span tends to be a multiple (about five times)[27] of the duration of the growth period, and also within the species, as will be discussed in connection with McCay's results. (In Fig. 18.9, k is the constant of equation (16.12), representing the rate of approach to the mature weight, A; the higher the value of k the more rapid the approach to maturity, that is, the shorter the duration of the growth period.) The problem of the influence of rate of maturation on the life span is complicated by the body-size factor; the rapidly maturing species usually has the smaller body size and, therefore, the higher metabolism per unit weight.

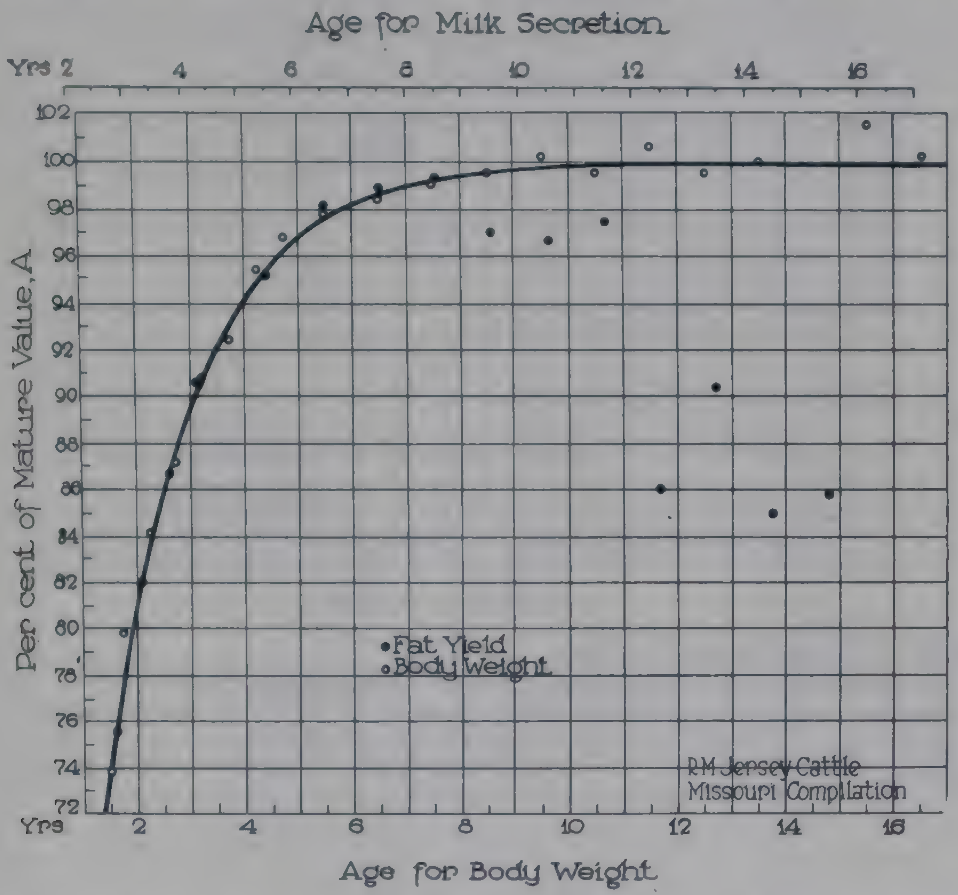

Fig. 18.18. Until age 7 years, body weight and milk yield follow the same course as demonstrated by the excellent agreement between the age curves for body weight and for milk yield (expressed in terms of butterfat yield). To avoid the confusion of separate axes for absolute values of weight and butterfat yield, the values were plotted in terms of percentages of the mature values. The numerical data for the weights and yields are given in Missouri Res. Bull. 96.

[27] Flourens, M. J. P., "De la longévite humaine et de la quantité de vie sur la globe," Paris, 1855. Buffon, G. L. C., "Histoire naturelle générale et particulaire," 1749. Bunge, G., "Wachstumgeschwindigkeit und Lebensdauer der Saugethiere," *Pfluger's. Arch. ges. Physiol.*, **95,** 606 (1903). Bell, E. D., "Mammalian longevity," *Nature*, **59,** 486 (1898). Lankaster, R., "Longevity of man and lower animals," London, 1870. Mitchell, P. C., "Longevity and relative viability in mammals and birds," *Proc. Zool. Soc. London*, 425 (1911). Flower, S. S., "Duration of life in vertebrates," *Id.*, pp. 247, 269, 911, 1865 (1925); p. 145 (1931); p. 265 (1935); p. 369 (1936); p. 1 (1937); p. 195 (1938).

18.2.1: Longevity and muscular exercise. Muscular exercise necessarily increases the metabolic rate, and if it exceeds a certain level it should accelerate the aging rate. Evidence substantiates this inference, especially

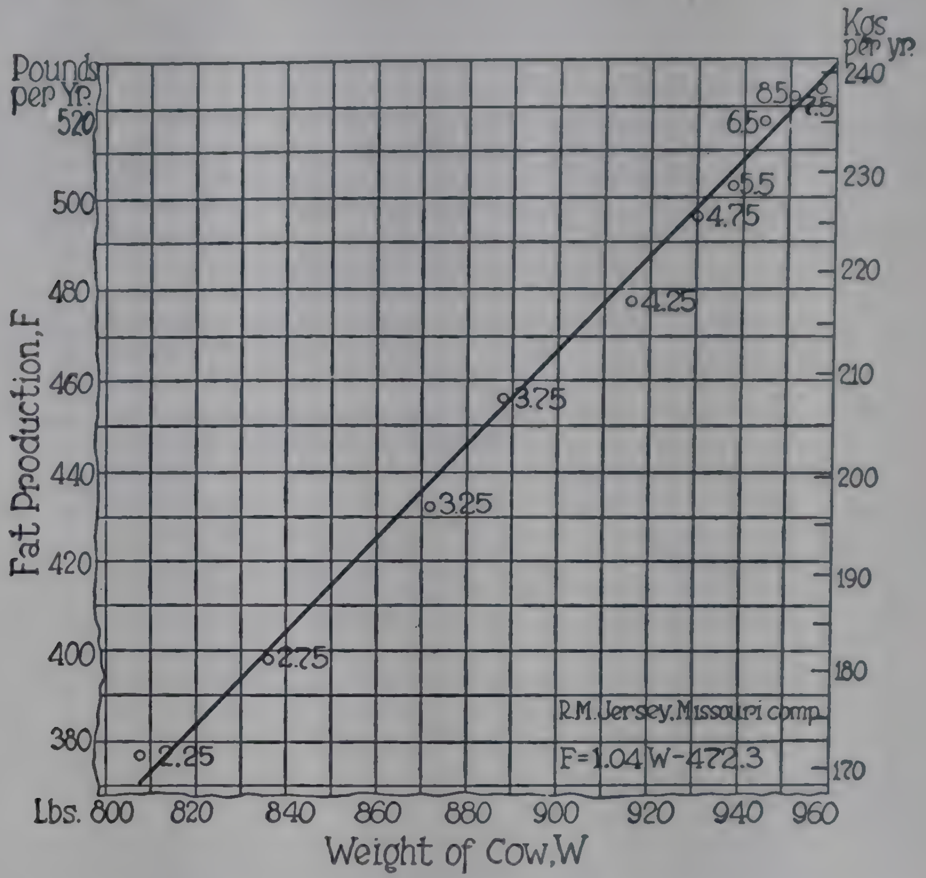

Fig. 18.19. The relation between body weight and butterfat yield during the period of growth (2.25 to 8.5 years). The equation indicates that an increase in body weight by one pound is accomplished by an increase in butterfat yield by 1.04 pounds per year. The mammary function and the body weight follow the same course during this period of the life cycle.

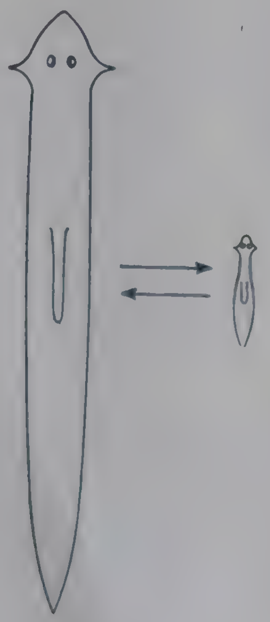

Fig. 18.20. Diagrammatic illustration of growth and senescence as reversible processes, modified from Child.

for exercise following middle age.[28] Slonaker[29] reported that rats having access to revolving drums for *voluntary* exercise ran about 5500 miles during life and *lived about 30 months;* control rats which had no access to revolving drums *lived about 40 months.* This observation needs confirmation, especially on dogs and horses.

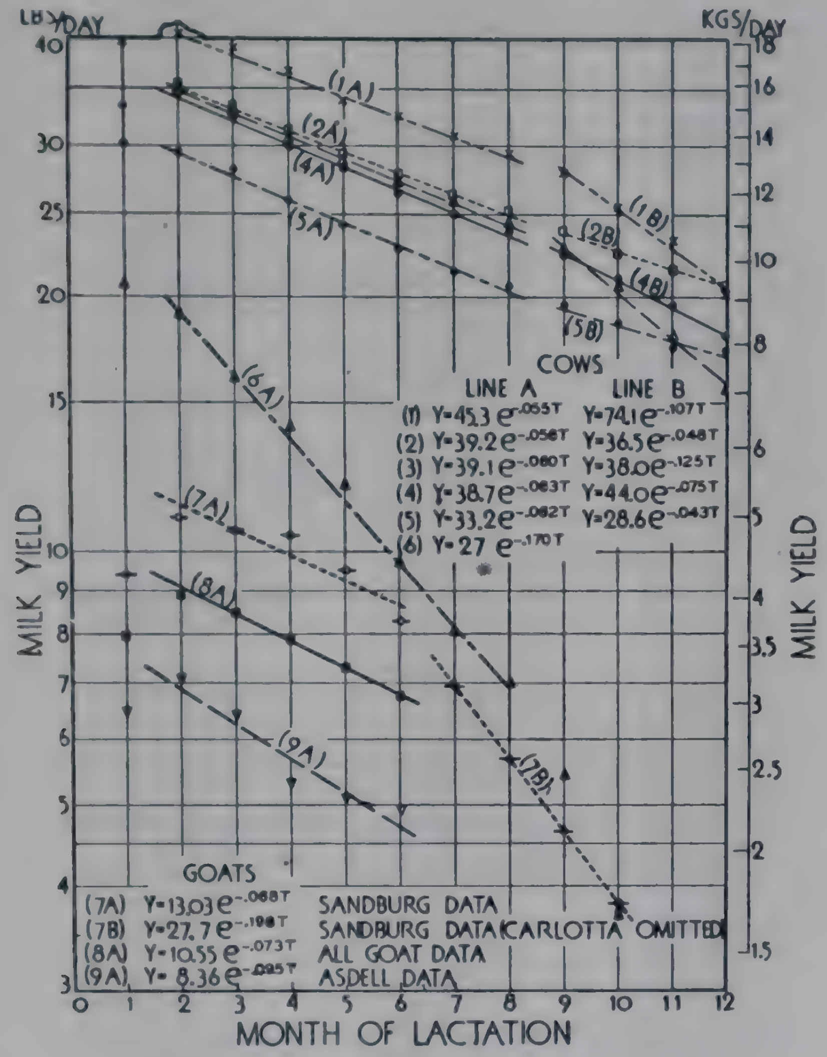

Fig. 18.21. A comparison of the declines in milk production in cows (curves 1, 2, 4, 5, 6) and goats (curves 7, 8, 9) plotted on arithlog paper. There is a break in some curves, due to pregnancy between 6 and 9 months in cows, and 6 to 7 months in goats. The curves preceding the break are indicated by A, and those following the break by B. The exponents multiplied by 100 represent the monthly percentage declines in milk production, which are seen to range (for segments A) from 5.5 to 17 per cent for cows, and from 6.8 per cent to 19.6 per cent for goats.

Human mortality data tend to substantiate the inference that hard muscular work is probably associated with early mortality. Thus, according to Dublin and Lotka,[30] unskilled manual workers have a mortality rate of 13 per 1000 as contrasted to almost half, 7 per 1000, for the professional and executive classes, who presumably do not work so hard physically. No doubt poorer nutrition and other factors of hygiene and perhaps even heredity may contribute to this striking mortality difference. This is indicated by the fact that agricultural laborers have a lower death rate (8) than unskilled city laborers (13), and that the rural life expectancy is 62 and 65 (for men and women, respectively) as contrasted to 57 and 61 for urban life expectancy.

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[28] *Cf.* Pearl, R., "The Biology of Death," Philadelphia, 1922. "The Rate of Living," New York, 1928. "Research proves that hard work does kill," *New York Times*, Sept. 7, 1924.

[29] Slonaker, J. R., "The normal activity of the albino rat and its rate of growth and duration of life," *J. Animal Behavior*, **2**, 20 (1912).

[30] Dublin, L. I., and Lotka, A. J., "Span of Life," New York, 1936.

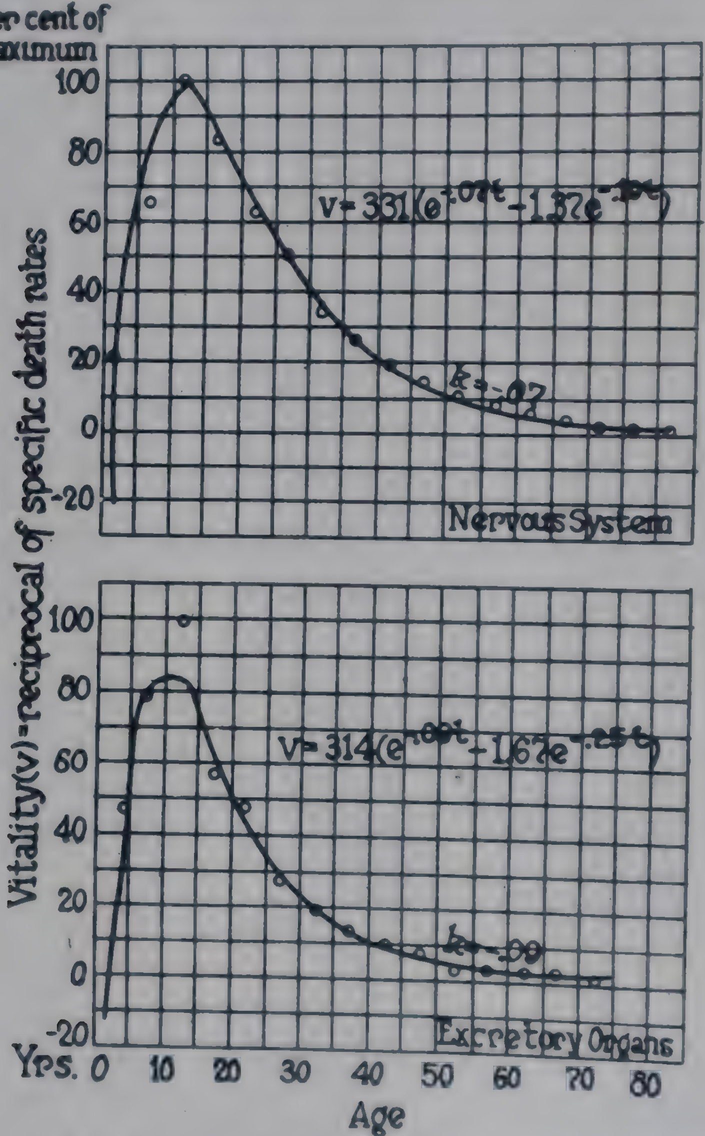

Fig. 18.22. The rise and decline of "vitality" in man (U. S. Registration area) with increasing age as measured by the breakdown of the nervous system, and excretory system. The data are represented as percentages of the maximum values. See Fig. 18.12 for the mortality data.

18.2.2: Longevity and temperature. Increasing temperature increases the metabolic rates of cold-blooded animals (Ch. 11, Fig. 11.1) and therefore increases the rates of growth and of senescence. Hibernation states of various types[31] decrease the metabolic rates and consequently prolong life. This accords with the colloidal theory. The metabolism of warm-blooded animals is oppositely affected by temperature below a certain optimal level: the lower the temperature the higher the metabolic rate (Figs. 11.1 and 11.11), and one would infer the more rapid the aging rate. This inference needs to be tested on warm-blooded animals by housing such animals as mice and rats at various temperatures.

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[31] For prolonging life in lower animals by desiccation, see Conklin, E. G., "The size of organisms and of their constituent parts in relation to longevity, senescence and rejuvenescence," *Pop. Sci. Monthly*, **83**, 197 (1913).

18.2.3: Longevity and the neuro-endocrine complex. High excitability due to genetic,[32] endocrine,[33] psychologic,[34] and other peculiarities may accelerate the aging rate by increased metabolic tempo directly and indirectly (as by action on the circulatory system). The neuro-endocrine complex may thus influence the longevity complex.

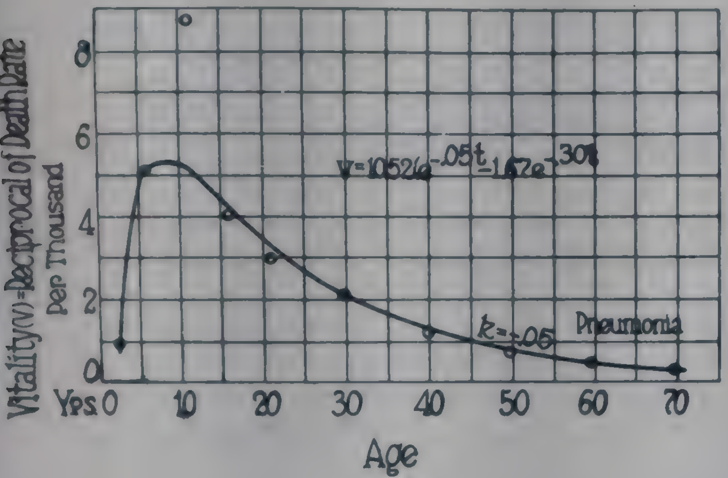

Fig. 18.23. The rise and decline of "vitality" with age in man (U. S. Registration Area) as measured by the reciprocals of death rate, due to pneumonia.

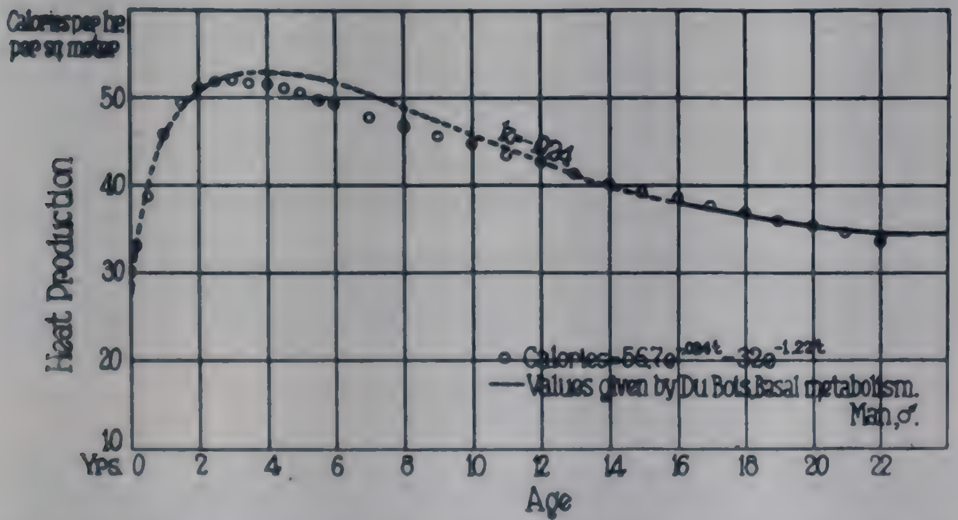

Fig. 18.24. The rise and decline of basal metabolism with increasing age in early life. (See chap. 14.)

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[32] Yeakel, E. H., and Rhoades, R. P., "Body and endocrine glands of emotional and non-emotional rats," *Endocrinology*, **28**, 337 (1941).

[33] *Cf.* Brown, W. T., and Gildea, E. F., *Am. J. Psychiat.*, **94**, 59 (1937). Sloan, E. P., "The Thyroid," Springfield, Ill., (C. C. Thomas), 1936. Dunbar, H. F., "Emotions and Bodily Changes," New York, 1935.

[34] Fulton, J. F., Editor, "The hypothalamus and autonomic function," Vol. 20, Assn. Res. Nerv. and Mental Dis., Baltimore, 1939.

Uncontrollable emotional behavior is observed clinically[35] as a result of brain abnormalities, and experimentally[36] following brain injury. Excitability often follows fatigue, worry, intoxication, and related factors which weaken the normal integrative control of the cerebral cortex.

Acute emotions are characterized by tense feelings and restlessness which profoundly affect visceral and other activities. Certain nerve excitations (parasympathetic, vagi, sacral) result in the production of excessive amounts of acetylcholine, sympathin, and histamine, which affect the heart, intestine, blood vessels, and skin, with consequent disturbances of various types.

Crile[37] has written eloquently from his great surgical experience in war and peace on the importance of emotions on the brain, thyroid, adrenal, celiac ganglion and sympathetic system (adrenal-sympathetic system) as "energy controller", and the burden they place on the cardio-vascular system. According to Crile, animals living in cold environment which are good conductors of heat (such as ocean water, 27 times as good a heat conductor as air), developed in the course of evolution particularly large brains

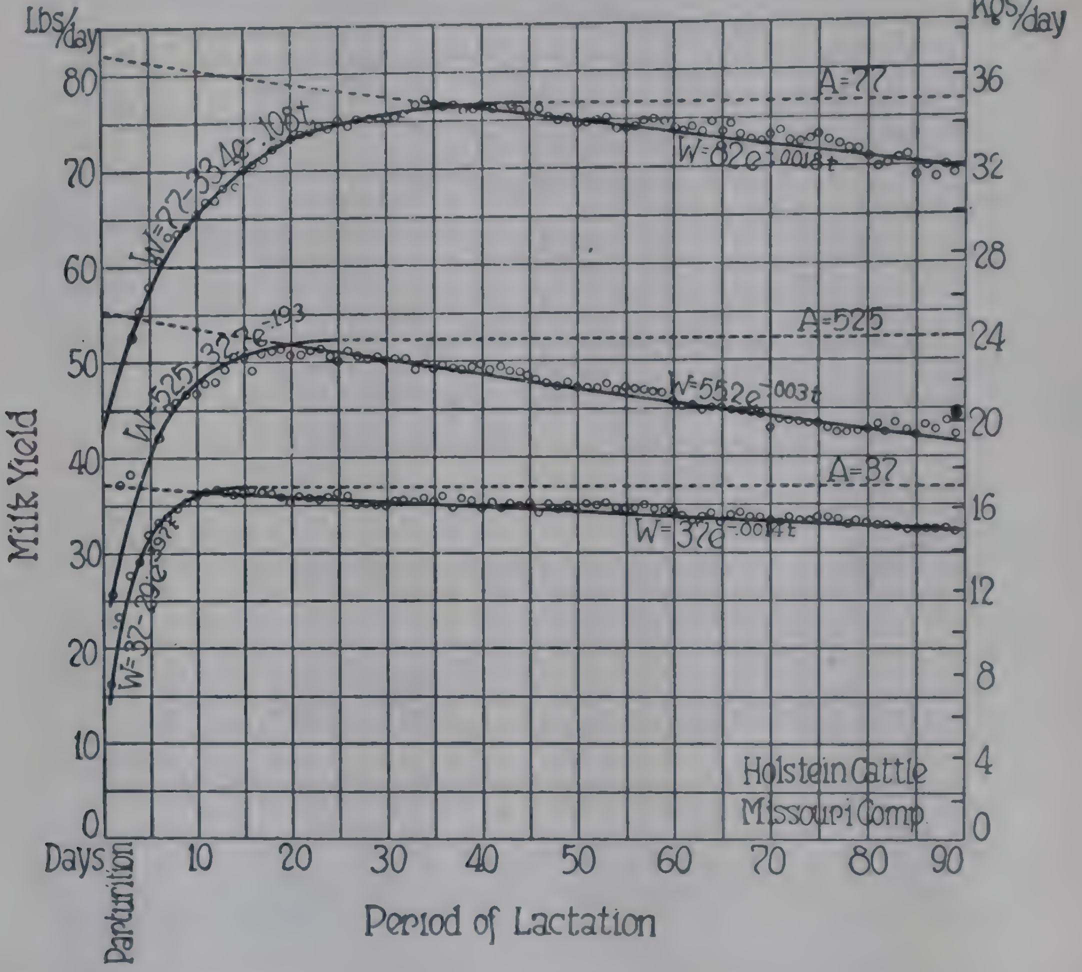

Fig. 18.25. The course of milk production with the advance of the period of lactation. This chart supplements Fig. 18.17, and illustrates the fit of one equation for the declining course of milk production, another for the rising course. The two equations are combined into one in Fig. 18.17.

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[35] *Cf.* Cushing, H., "Intracranial tumors," Springfield (Thomas), 1933.

[36] Cannon, W. B., and Britton, S. W., *Am. J. Physiol.*, **72**, 283 (1925). Bulatao, E., and Cannon, *Id.*, pp. 295, 313. (Removal of cortex from brain stem in cats led to development of violent emotional outbursts on the slightest provocation. There was lashing of tail, arching of trunk, clawing, biting, etc., accompanied by signs of vigorous sympathetic discharge as indicated by erection of hair, sweating of toe pads, dilation of pupils, increase in blood sugar up to five times normal.)

[37] Crile, George, "A neuro-endocrine formula for civilized man." The Educational Record Supplement, Jan. 1941, Am. Council Education, Washington, D. C.

and thyroids to keep the heat generation at a high level. A socially or psychologically overstimulating environment may produce a somewhat similar, but in this case pathological, syndrome. Thus exophthalmic goiter, characterized by enormously high energy and protein metabolism, is peculiar to civilized man. "The brain-thyroid axis is destroying many of our most brilliant men and women through a pathologic physiology of oxidation called exophthalmic goiter and also through neuro-circulatory asthenia, or 'soldier's heart'. The axis partner of the brain, the faithful heart, is reaching its ceiling of possibilities".[37]

Some emotions are acute, such as those investigated especially by Cannon in relation to the sympathetico-adrenal system;[38] others are chronic or conditioned, such as those investigated by Pavlov.[39]

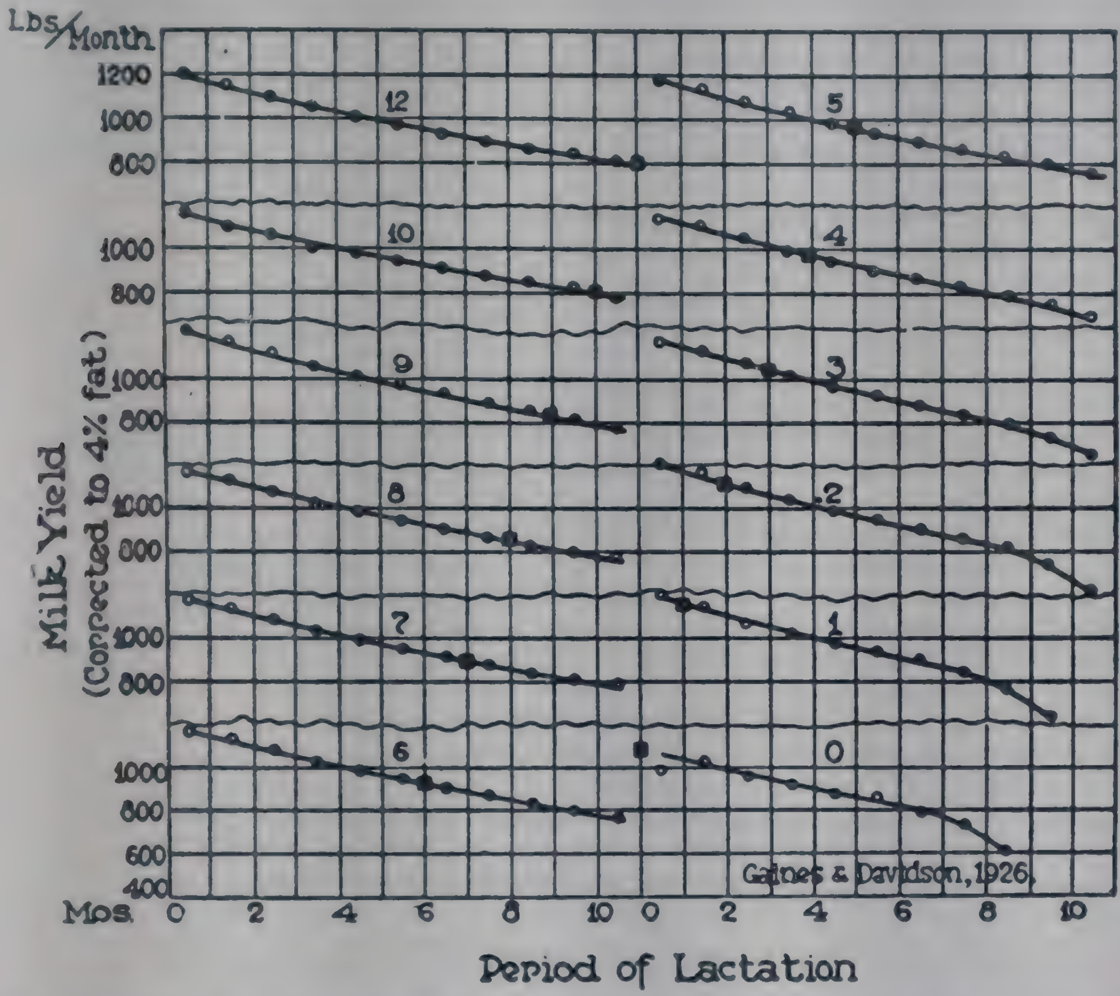

Fig. 18.26. To illustrate the effect of gestation on the course of milk production with the advance of the period of lactation. The rectangles and numerals indicate the month at which the cows were bred. The earlier the breeding the greater the decline in milk production at the end of the year. Compare to Figs. 18.21, 18.27, and 18.30.

What was said about man is true of animals. Good animal husbandmen appreciate the importance of gentle treatment of their animals, and are aware of the unpleasant conditioned reflexes that may develop, especially in horses and dairy cattle.

The division of causes of death into external and internal is thus somewhat arbitrary. Internal causes, such as those due to the aging of the cardiovascular-renal system, are influenced by the endocrine and nervous activities, which in turn are influenced by psychosocial and other factors and indeed by the nature of the thoughts, which are partly under control. As years roll on, from birth to old age, the individual "is reacting to social life . . . with feelings of emotions which . . . influence bodily functions and may give rise to functional impairment and eventually to structural damage. . . . Worry, anxiety, and unhappiness may accelerate functional decline and aggravate the impairments of later life".[40] If just the feeling of being old can lead to a diminution of functional activities, is it possible to delay aging by continuing life activities and maintaining a feeling of competence for life?"[40]

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[38] Cannon, W. B., "Bodily changes in pain, hunger, fear and rage," New York, 1929 and 1934. Cannon, "The wisdom of the body," New York, 1932. Cannon, "The James-Lange theory of emotion," *Am. J. Psychol.*, **39**, 106 (1927).

[39] Pavlov, I. P., "Conditioned reflexes," London, 1927.

Some of these ideas need to be worked out quantitatively by controlled experiments on laboratory animals by subjecting them to various psychologic factors (as fright) and following the metabolic levels and longevity; also by investigating the influence of various levels of thyroxine administration and thyroidectomy on metabolic levels and longevity. Similar investigations suggest themselves on the adrenals (administration of adrenaline, cortin, irradiating the adrenals, etc.) and on parts of the nervous system.

Neuro-endocrine research in relation to aging is a virgin field. The thyroid is perhaps the only endocrine that has been at all investigated in this relation.[41] Very little is known about its function in aging.[42] The histology of the thyroid indicates both decrease and increase in activities with advancing age[43]. Some characteristics of old age resemble those of hypothyroidism.[42] The respiration rate of thyroid tissue declines with increasing age,[44] but a given dose of thyroxine or thyrotropic hormone has a greater metabolic effect on the old then young.[41] Dogliotti[45] believes that the activity of the thyroid often increases with increasing age, and Cowdry[46] noted that the thyroid in a

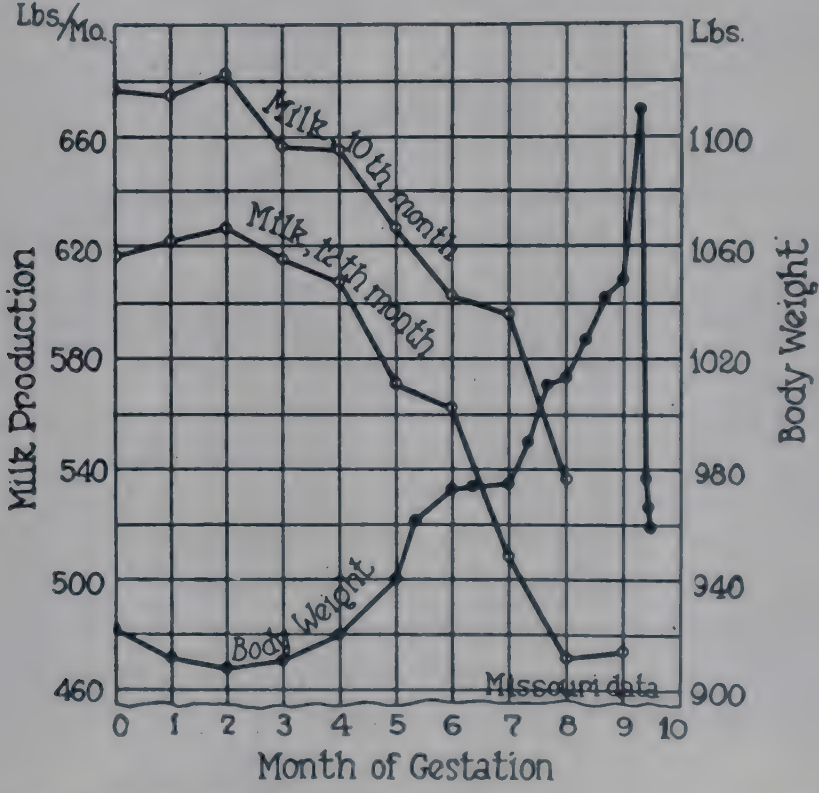

Fig. 18.27. Another illustration of the influence of the stage of *gestation*, on the course of milk production with the advance of the period of lactation.

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[40] Frank, L. K., "The problem of ageing," Club for research on ageing. Washington, D. C., Jan. 12–13, 1940.

[41] **See Magnus-Levy, 1895, and other references in Sect. 7.4.**

[42] Carlson, A. J., *in* "Problems of Ageing," p. 361.

[43] Cooper, E. R. A., "The histology of the more important human endocrine organs at various ages," *Oxford Med. Pub.*, 1935. Parsons, R. J., Medical papers, dedicated to H. A. Christian, Baltimore, 366, 1936. Loeb, L., and Simpson, R. M., *Science*, **88**, 433 (1938). Thompson, W. O., "The endocrine problems in later life." *Med. Clin. of North America*, **24**, 79 (1940).

[44] **Belasco, I. J., and Murlin, J. R., *Endocrinology*, 28, 145 (1941).** Belasco, I. J., *Id.*, p. 153.

[45] Dogliotti, G. C., and Nuti, G. N., *Endocrinology*, **19**, 289 (1935).

[46] **Cowdry, E. V., "A Text book of histology," Fig. 96, p. 204.**

111-year woman was in excellent condition. There are many such scattered observations in the literature on the age behavior of endocrines which are difficult to interpret because of their widespread interrelations. The involution of the thyroid (hypothyroidism) during aging may be the result of the aging of the body as a whole, and there is no reason for *a priori* assumption that thyroid administration would retard the general involutional process. Data are needed on this problem.

18.2.4: Longevity and diet. Overweight certainly reduces the expectancy of life, both in rats[47] and in man.[48] One possible unfavorable factor is the increased energy metabolism associated with overfeeding (Ch. 4) and with carrying the extra weight of the overfed individuals. Then, too, excessive fat offers mechanical obstruction to the functioning of the visceral organs and

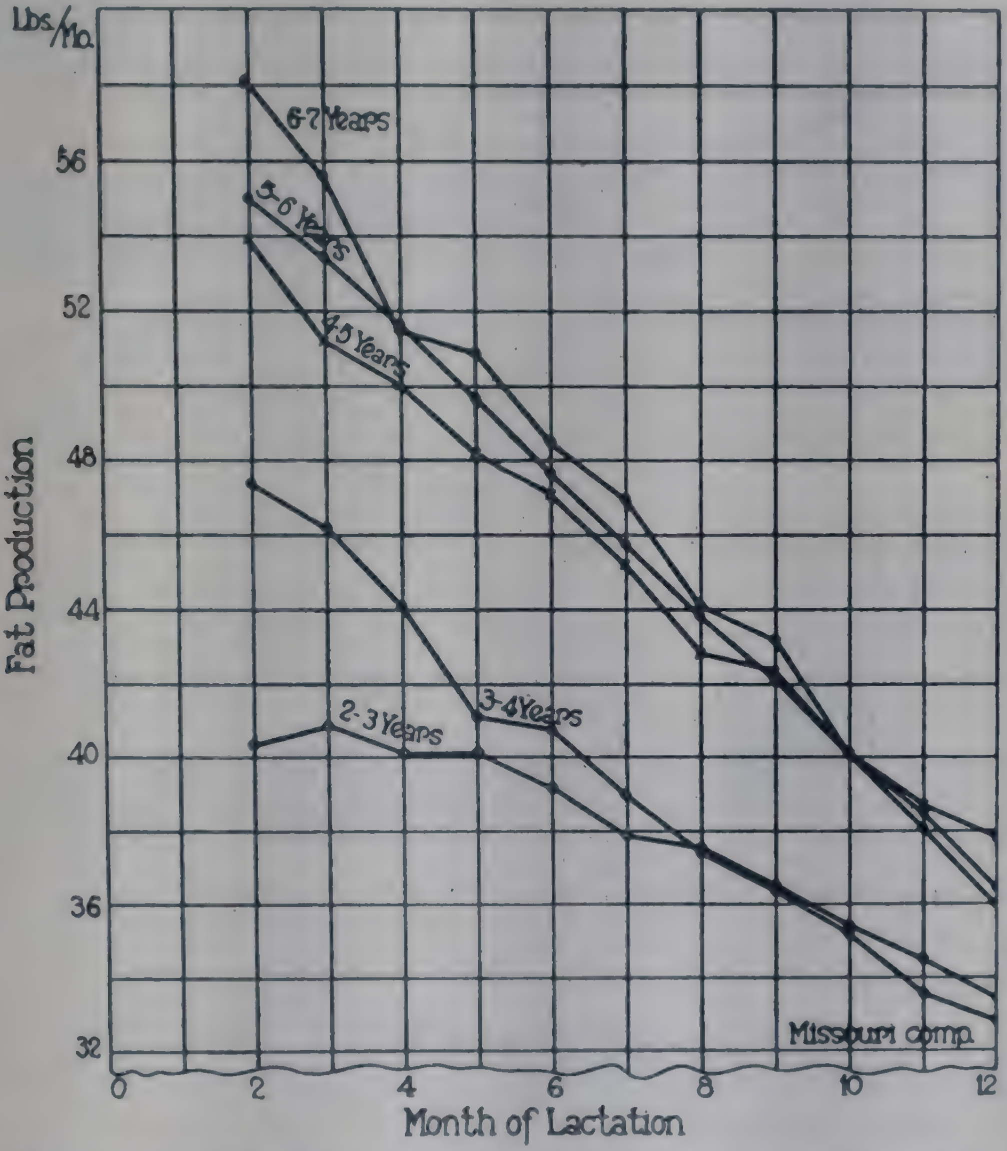

Fig. 18.28. Influence of age on the course of milk production with the advance of the period of lactation.

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[47] McCay, C. M., Maynard, L. A., Sperling, Gladys, and Osgood, H. S., "Nutritional requirements during the latter half of life," *J. Nut.*, **21**, 45 (1941). For the earlier papers, see McCay, Maynard, *et al.*, "Growth of trout," *J. Nut.*, **1**, 233 (1929); Cellulose in the diet, *Id.*, **8**, 435 (1934); "Ageing after retarded growth," *Id.*, **10**, 63 (1935), and **18, 1** (1939).

[48] Dublin, L. I., and Lotka, A. J., "Length of life," New York, 1936.

to the free movement of the muscles in the conduct of the business of living, thus increasing the energy cost of their performances.

One of the possible dangers of overfeeding with certain foods is of a somewhat different nature, namely, deposition of lipoids, especially cholesterol, in the blood vessels, especially the coronary arteries, thereby reducing the rate of blood flow to the heart muscle, and often causing sudden death by a loosened lipoid fragment[49] and by thrombosis.

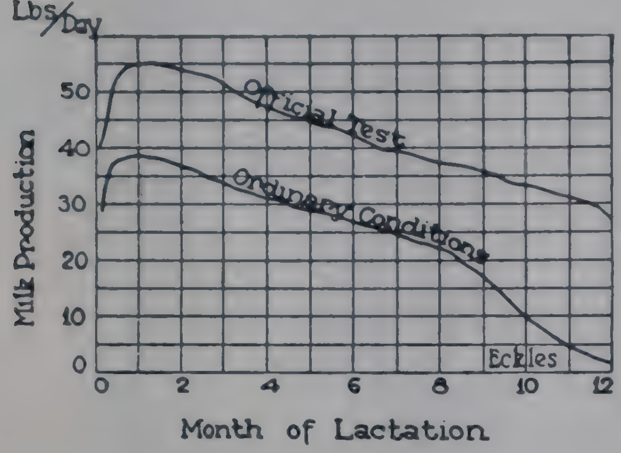

Fig. 18.29. Official test cows are bred later, therefore, do not show the depressing effect of gestation as the non-test cows.

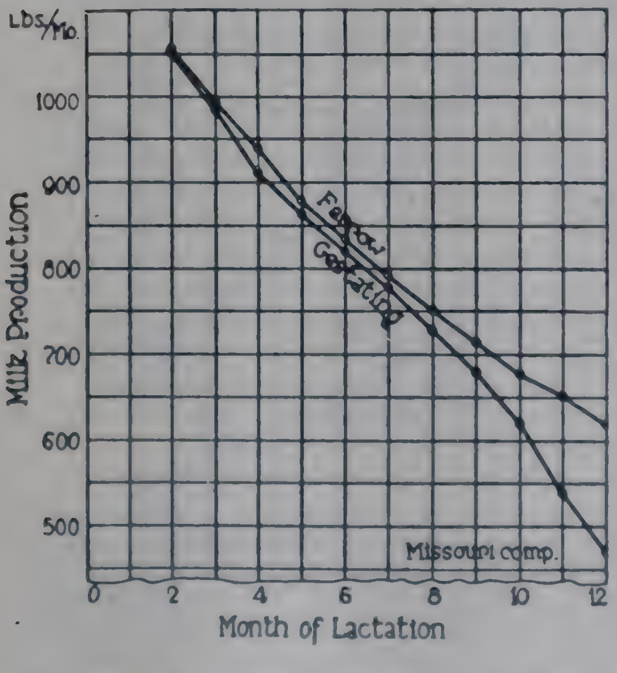

Fig. 18.30. Comparison of the course of milk production in farrow and gestating cows.

Overfeeding, especially on carbohydrates, is thought to hypertrophy the pancreatic islets with hyperinsulinism, establishing a vicious circle. The more food, the greater the hyperinsulinism, and the greater the hyperinsulinism, the greater craving for food, with resulting obesity. The hypertrophy of the islets is then followed by their degeneration and diabetes.[50]

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[49] Leary, Timothy, "Experimental artherosclerosis in the rabbit compared with human (coronary) experimental atherosclerosis," *Arch. Path.*, **17**, 453 (1934). Cowdry, E. V., Editor, "Arteriosclerosis," New York, 1933.

[50] Hess, W. N., *Anat. Rec.*, **57**, Sup. p. 37 (1933). Brody, S., *Ann. Rev. Bioc.*, **4**, 383 (1935).

The above discussion on deleterious effects of overfeeding was concerned with the energy aspects of overfeeding on calories. With the possible exception of excessive intake of vitamins A and D, there is, perhaps, no danger of overfeeding vitamins.[51] There is certainly no danger from excessive vitamin intake from vitamin-rich *natural* mixed foods, and, normally, this is the form in which vitamins should be taken. Vitamin intake should, on the contrary, increase with increasing age to compensate for reduced absorption,[52] utilization and storage, and greater needs for detoxification (Ch. 6), and especially because of the declining oxygen supply to the tissues, which may be compensated in part by increasing the concentration of the oxidation enzymes (vitamins) in the body. The ideal diet for the aged should then be relatively

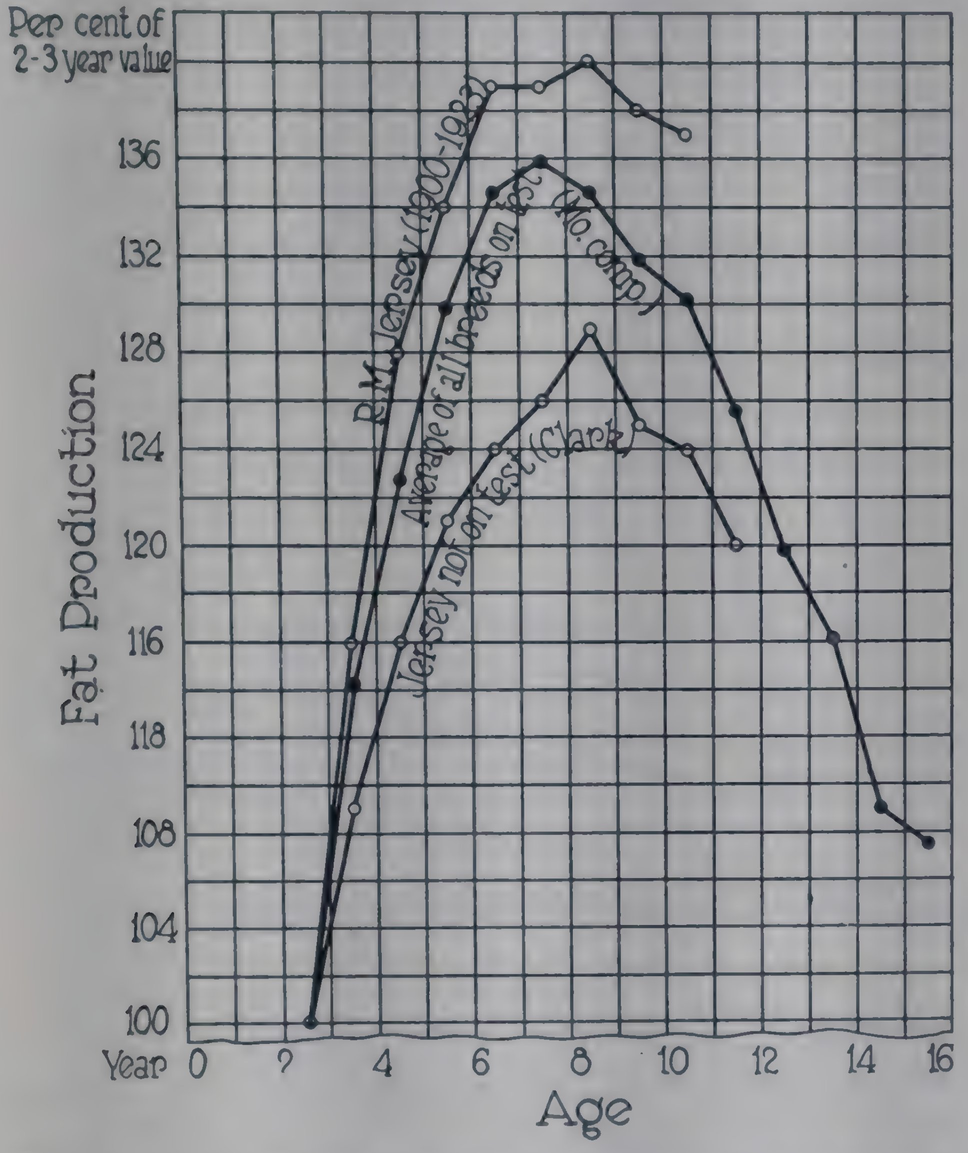

Fig. 18.31. Age course of milk production as percentage of the 2–3 year level. These are averages of different animals at different ages.

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[51] Molitor, H., *Fed. Proc.*, **1**, 309 (1942).

[52] *Cf.* Irving, J. T., and Richards, M. B., "Influence of age on vitamin A requirements," *Nature*, **144**, 908 (1939). Kruse, H. D., *U. S. Public Health Reports*, **156**, 1301 (1941).

poor in calories and liberal in vitamins and other supplementary foods (Sects. 20.5–20.6).

Sherman[53] reported favorable effects on longevity and growth of liberal supplements of vitamin A, riboflavin, calcium, and related factors found in milk, even when superimposed on an already good diet. Thus, rats fed for 8 generations on a diet of one-third whole milk powder and two-thirds whole wheat reproduced and grew better and also lived longer than rats fed on a diet of one-sixth whole milk powder and five-sixths whole wheat. This illustrates Sherman's "principle of the nutritional improvability of the normal".

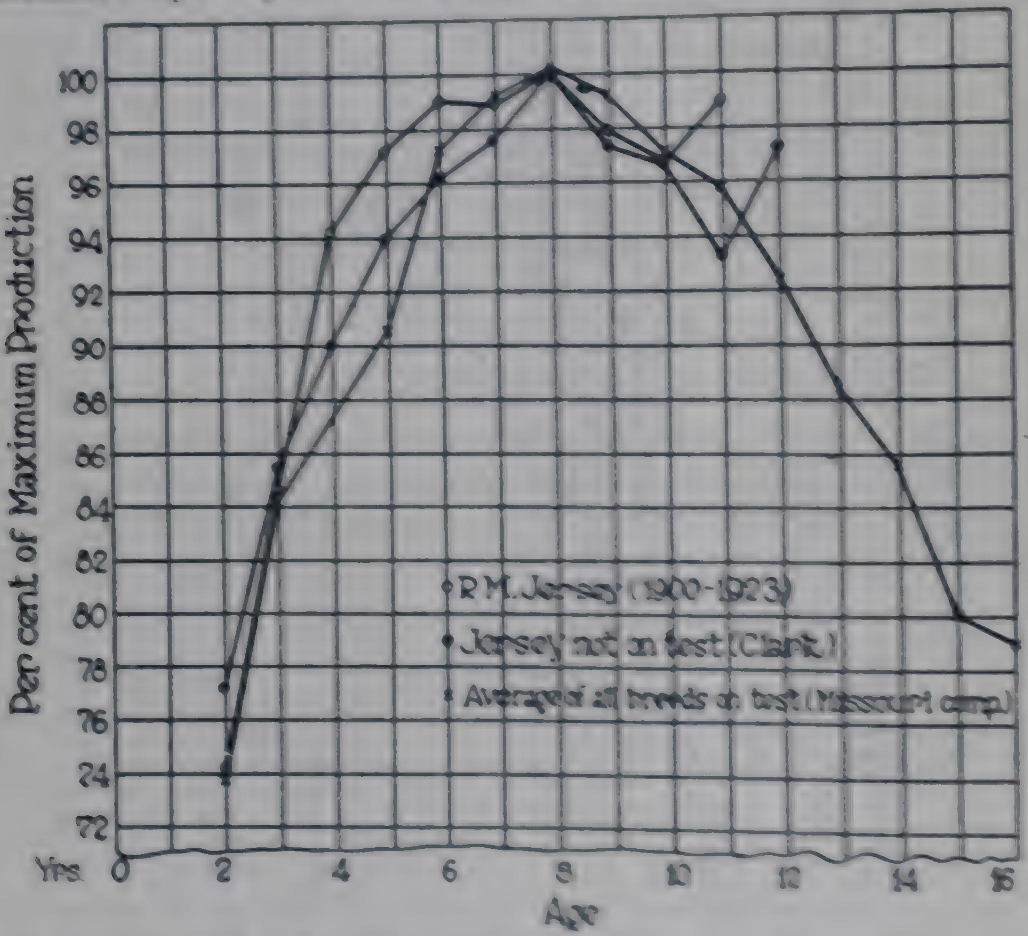

Fig. 18.32. Age course of milk production as percentage of the maximum production.

McCay[54] and associates reported spectacular data on the influence of interrupting growth during certain age intervals, beginning shortly after weaning, on the life span, as illustrated by the following table.

Diet	Maximum life span, of rats (days)			
	Males	Increase	Females	Increase
Rapidly growing	896		985	
Retarded 300 days	1018	122	1183	198
" 500 "	1103	207	1078	93
" 700 "	1025	129	1320	335

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[53] Sherman, H. C., Campbell, H. L., *et al.*, "The influence of food upon longevity," *J. Nut.*, **2**, 415 (1930); **14**, [illegible] (1937), and **21**, 221 (1941). See also Sherman, *et al.*, *J. Biol. Chem.*, **60**, 5 (1924); **126**, [illegible] (1938); **137**, [illegible] (1941); *Proc. Nat. Acad. Sci.*, **14**, 83 (1928); **25**, 16 (1939), **27**, 280 (1941); News Edition, Am. Chem. Soc., **19**, [illegible] (1941).

Both the rapid and retarded-growth groups received the same quantities of basal ration diet, rich in protein, vitamins, and minerals, but not sufficient in calories to permit normal growth. The rapid or normal-growth group, therefore, received a starch-sugar-fat supplement to permit the rapid growth.

The *rapid-growth* group is seen to have had rather long-lived individuals, 896 and 985 days for males and females, respectively. The life span might, perhaps, have been greater if this group received the supplement in the form of the vitamin-rich basal ration instead of the special vitamin-poor starch-sugar-fat ration. The *retarded-growth* group attained phenomenal life spans of 1103 days for a male retarded 500 days and 1320 days for a female retarded 700 days.

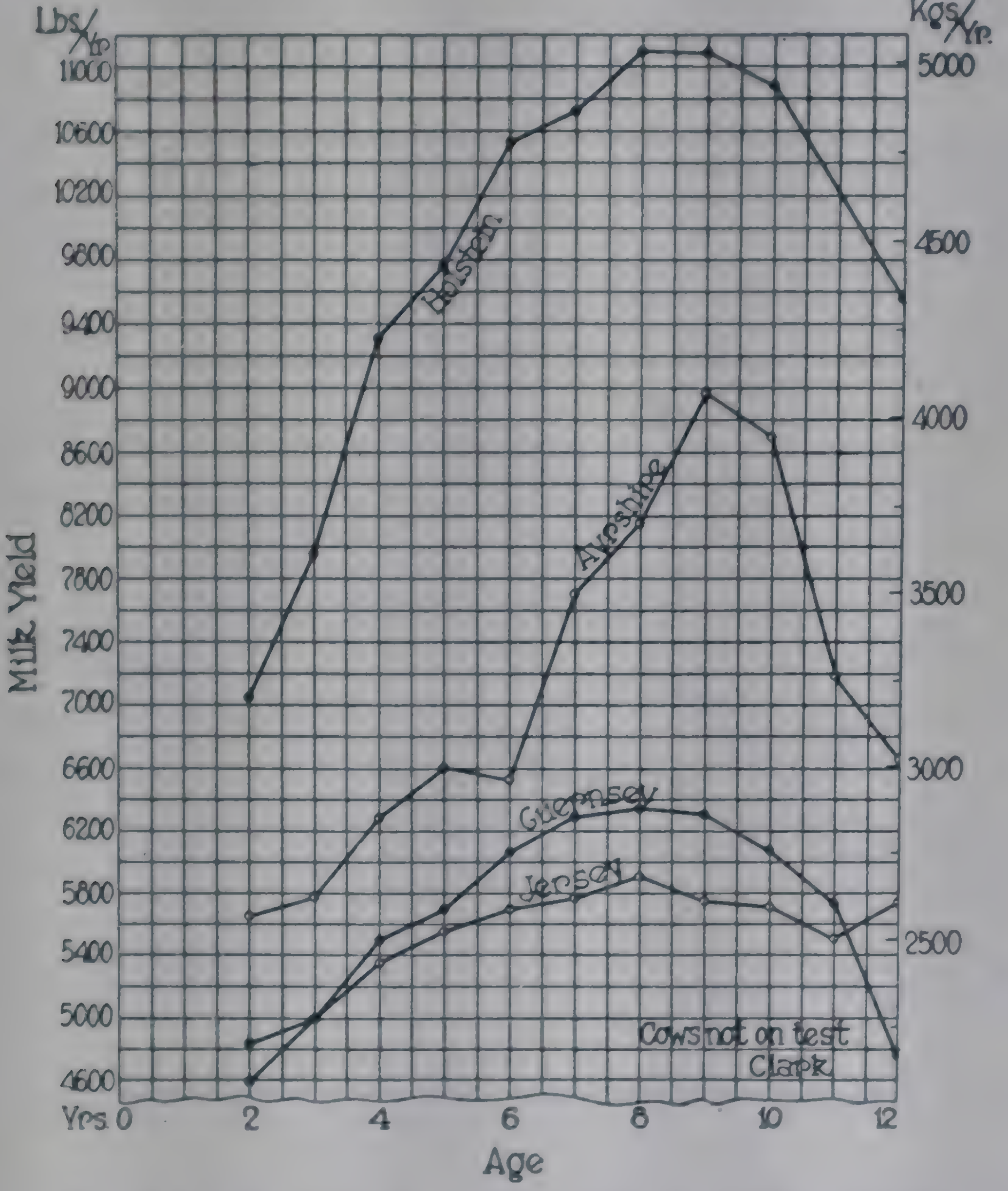

Fig. 18.33. Age course of milk production of cows not on test.

These striking results suggest several somewhat conflicting thoughts. The renewed growth following the 700-day caloric starvation may be in the nature of a new growth cycle, analogous to the second growth cycle of lactic-acid bacteria shown in Fig. 18.1b, which does not differ in length from the first growth cycle. One is tempted to say that for this female, which survived 1320 days, life began at 700 days! This thought is in harmony with the colloidal aging theory according to which the life span is correlated with the length of the growth period (Fig. 18.9). One wonders whether the renewal of growth in weight following the 700-day retardation was also accompanied by initiating of sex activity.[54]

One is reminded in this connection of Hartman's amoeba, kept alive and youthful for four months by repeatedly cutting off part of the body which continued regeneration; and of Child's planarian[55] (Fig. 18.20) which reverted to the immature form on starvation, then again to the mature form on refeeding; and of Carlson's or Child's remark that a period of fasting gives one a feeling of exhiliration during the refeeding period.

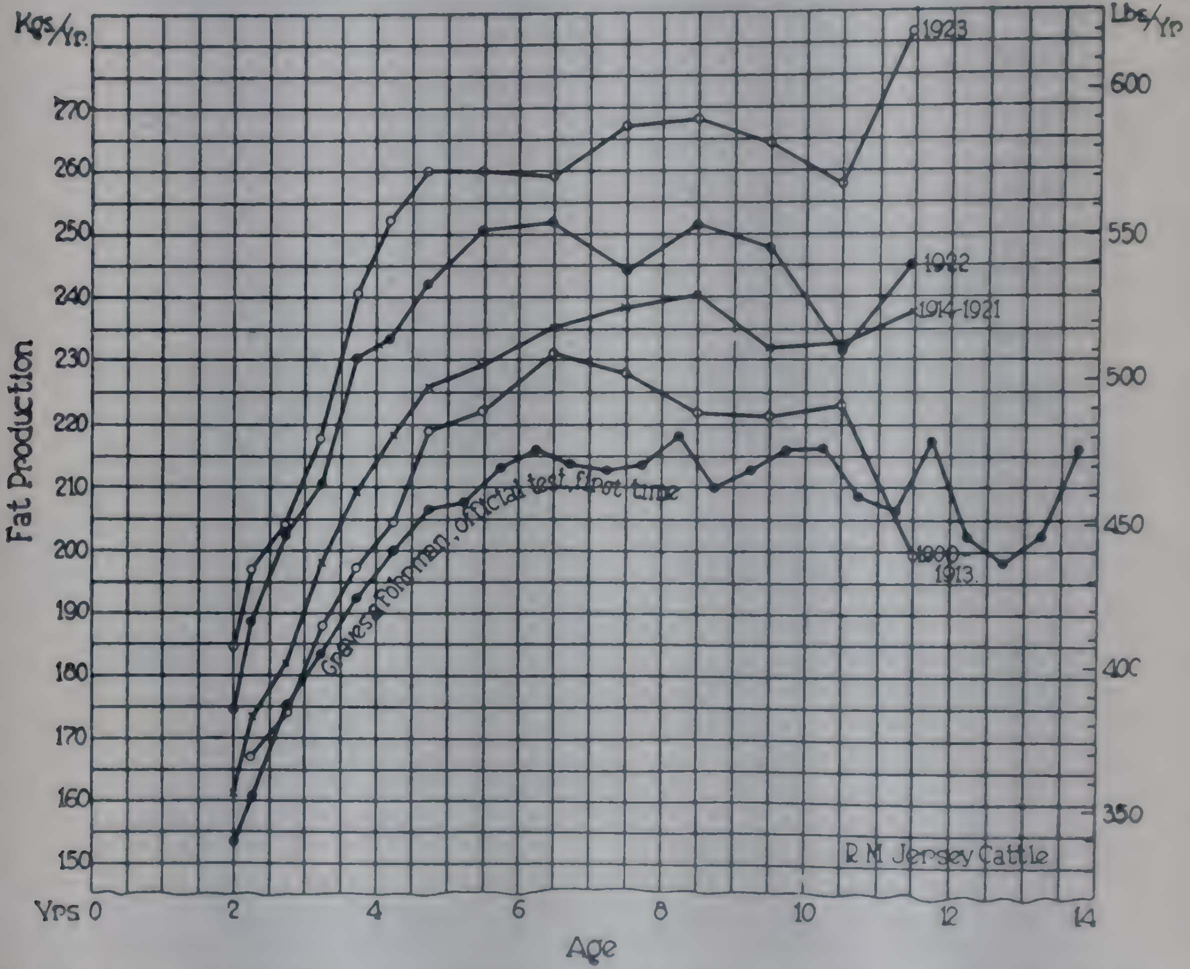

Fig. 18.34. Progressive improvement of Register of Merit Jersey cattle in the United States.

These results do not necessarily imply that growth retardation or periodic fasting are desirable practices; growth retardation and fasting may prolong the life of a few hardy individuals, but, perhaps, the number surviving such a regime under normal conditions is small. This thought may be presented by the following questions: (1) What would be the life span of the retarded-growth rats if they had been kept on this retarded-growth level until death? Did the initiation of the new growth cycle after the 500 or 700 days of caloric starvation prolong the mean and maximum life span, and if so by how much? (2) What were the specific mortalities (deaths per 100 living of the same age) at various ages—for 10-day intervals (comparable to the yearly mortality tables for man)—of (a) the rapid-growth and the retarded-growth rats? Perhaps only such exceptional animals as are able to survive the starvation period benefit in longevity by the starvation regime. (3) What would be the influence of changed environmental conditions on these survivorships (these animals were housed in air-conditioned rooms)?

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[54] Asdell, S. A., and Crowell, M. F., "Effect of retarded growth on sex activity." *J. Nut.*, **10,** 13 (1935).

[55] Child, C. M., "Senescence and rejuvenation," Chicago, 1915.

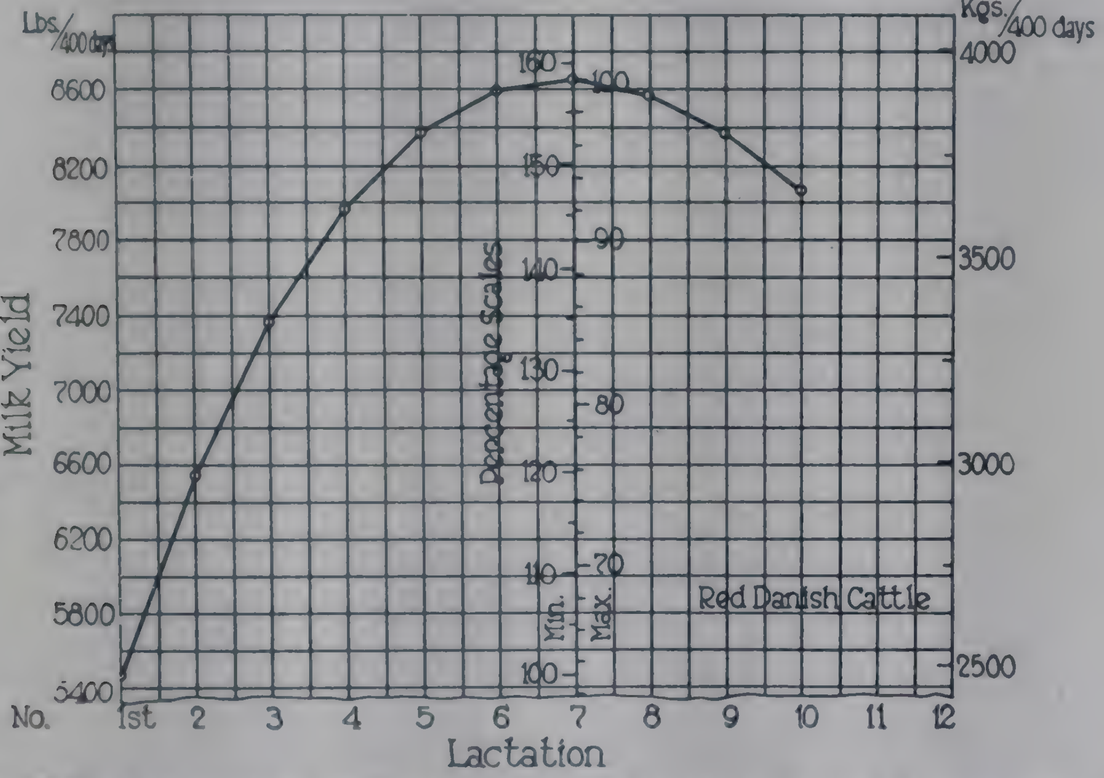

Fig. 18.35. Age course of milk production of the *same* 292 Red Danish cows. This is the only curve representing the same animals. The milk production is plotted against successive 400-day lactation periods, not calendar years.

From an evolutionary viewpoint one would not expect that severe growth retardation would benefit. Birth usually coincides with the beginning of the season of lush food supply (Ch. 8) favorable for rapid growth and fattening, in preparation for future rigors.

McCay's results are, of course, extremely interesting from the viewpoint of the colloidal theory of aging, individual and species differences in the power to resume growth after severe retardation[56] (Fig. 19.16), influence of environmental conditions on such survival, selective breeding of hardy stock, and related limiting problems in growth and senescence.

[56] See, for example, Osborne, T. B., and Mendel, L. B., "The resumption of growth after long continued failure to grow," *J. Biol. Chem.*, **23**, 439 (1915).

In summary, from the viewpoint of longevity, moderate rather than rapid growth, and in later life, a low-calorie, moderate-protein diet of good quality,

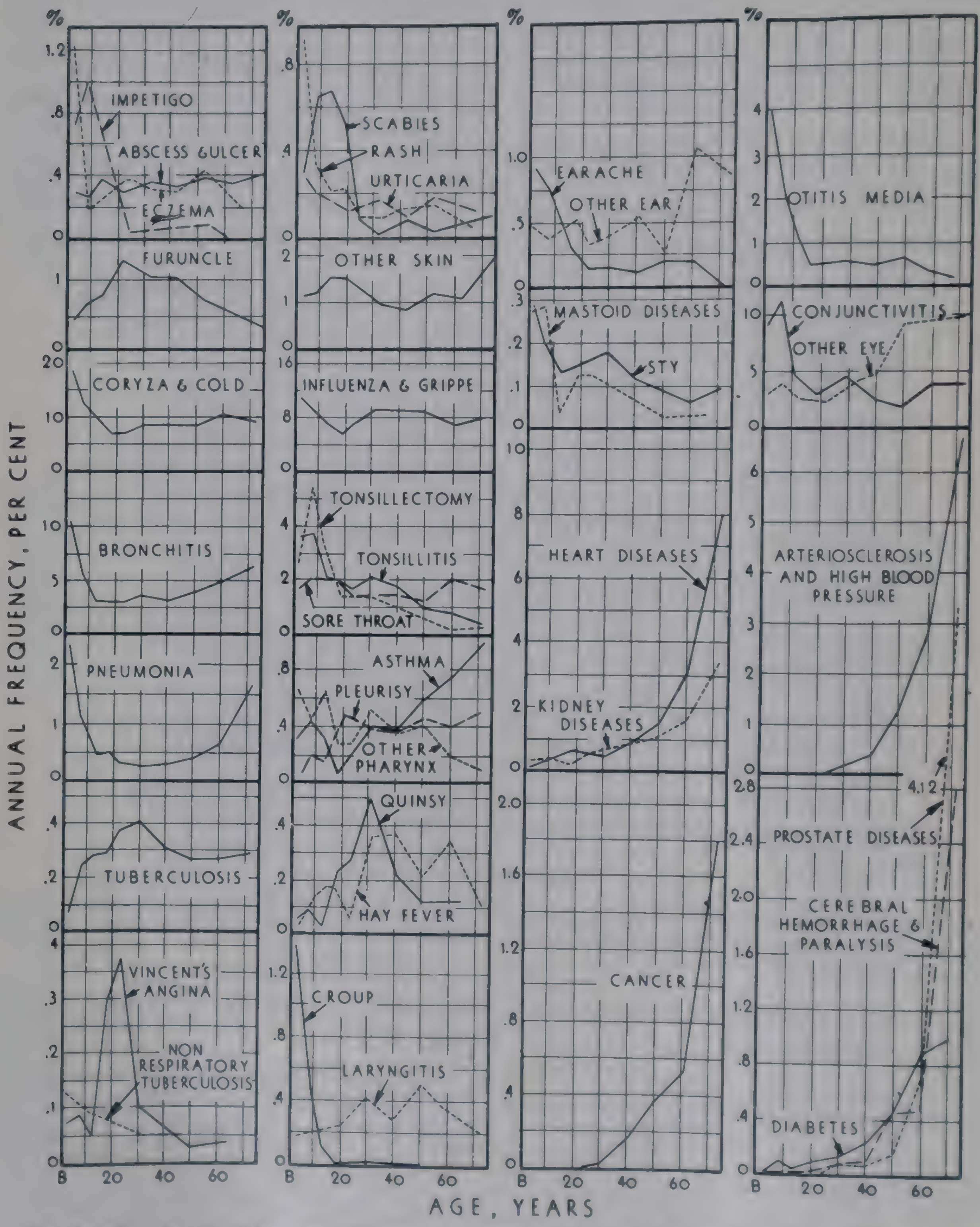

Fig. 18.36a. Age incidence of illness. "Based on records for 9000 families in 18 states visited periodically for 12 months, 1928–31." Replotted, for purpose of condensation, from charts by S. D. Collins *in Public Health Reports* for October 11, 1935, p. 1404. Incidence is in terms of annual cases per one hundred, that is in per cent per year. The curve on home accidents from R. H. Britten, J. Klebba, and D. E. Hailman, *Id.*, p. 2061, Nov. 8, (1940).

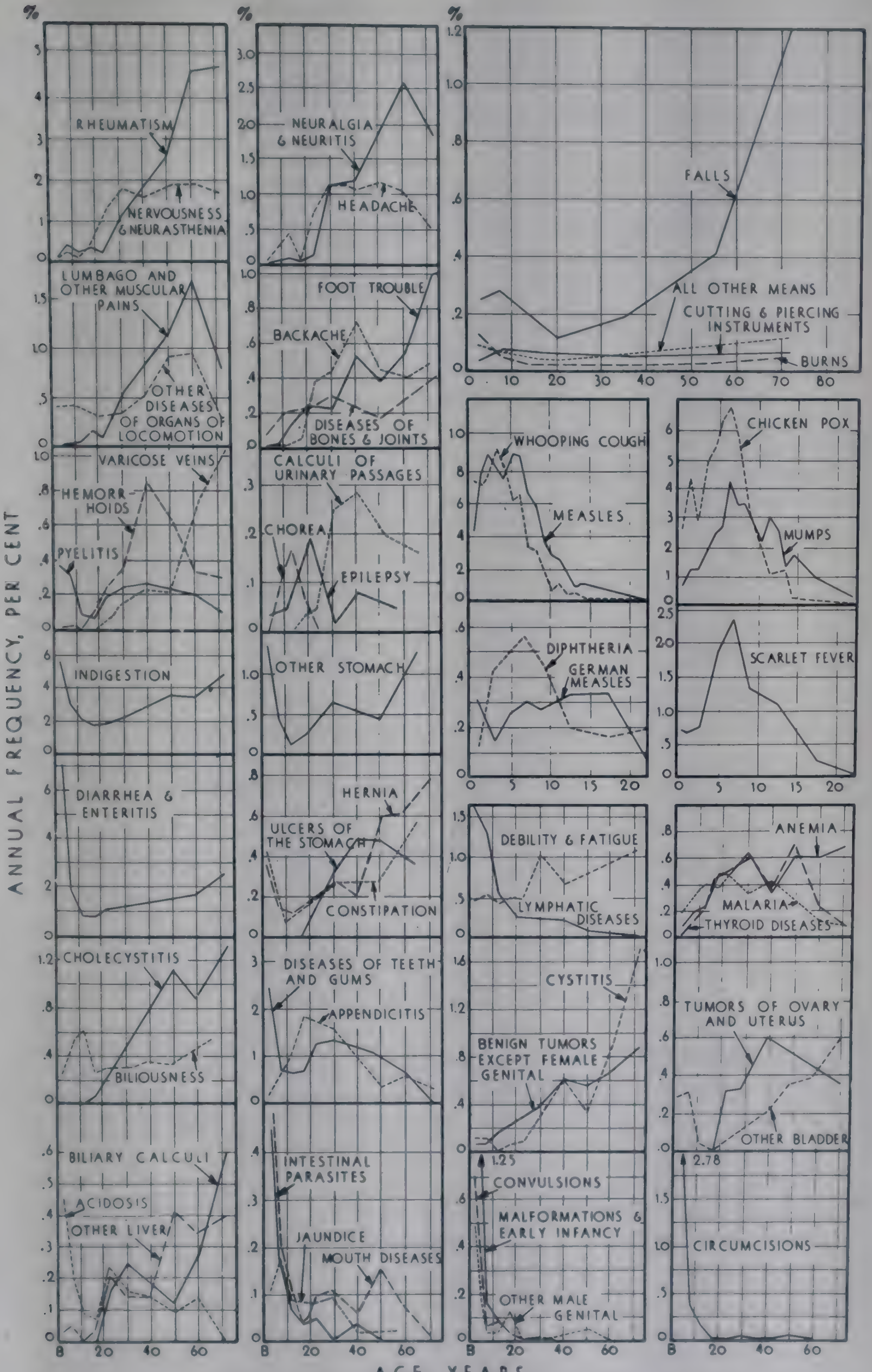

Fig. 18.36b. See legend for Fig. 18.36a.

with liberal vitamins,[57] and minerals seems best. From the viewpoint of immediate gross efficiency of productive processes, however, such as from the viewpoint of milk, meat, or egg production, high feed consumption and rapid growth may be more desirable in order to save maintenance and other overhead expenses.

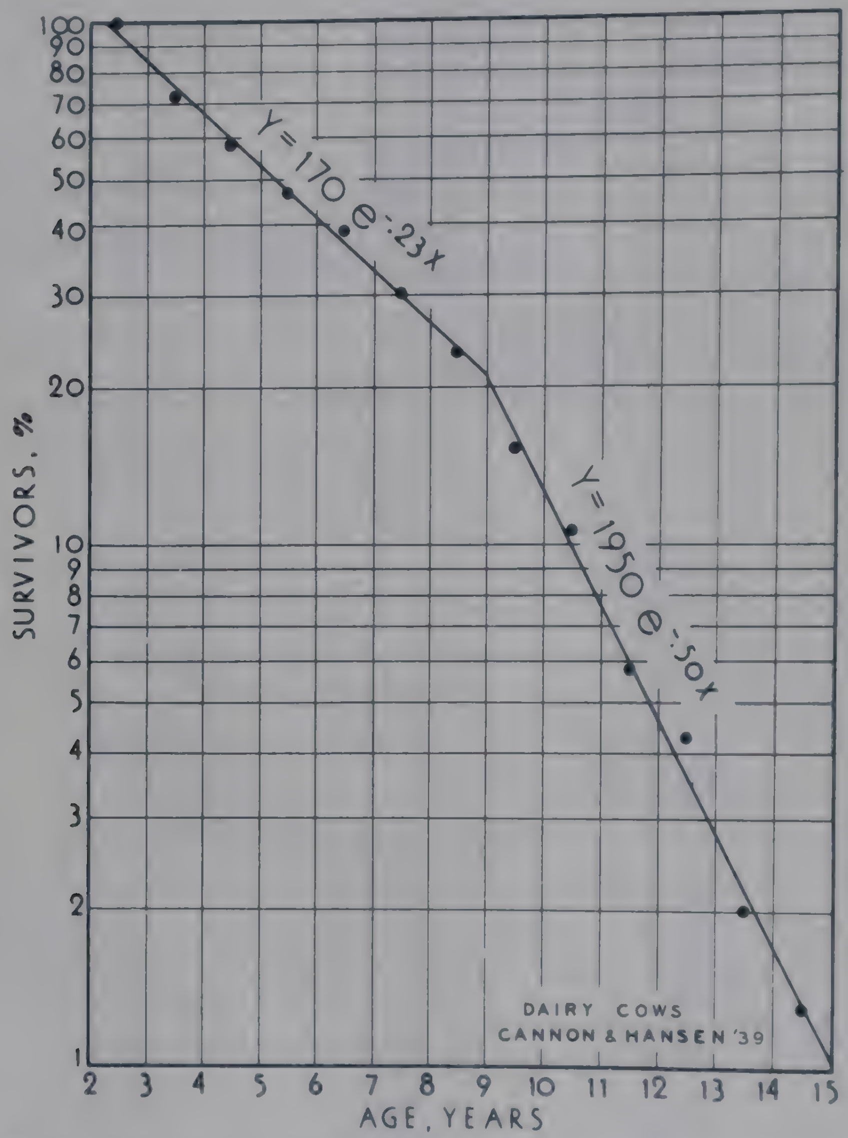

Fig. 18.37. Survivorship curves of dairy cattle, plotted from data by Cannon and Hansen, Iowa Agr. Exp. Sta. Bull., 1939. Some old cows now living: the Guernsey cow Vestview Violette, 164104, now 21 years of age, gave birth to 15 offspring, has a record of 16000 lb. milk or 655 lb. butterfat in a year; Mixter Golden Charm, 151351, 19 years, had 15 calves, record of 12000 lb. milk, 616 lb. butterfat (*Guernsey Breeder's J.*, p. 260, Feb. 15, (1942)).

18.3: Criteria of aging and the prime of life. It is difficult to deceive an experienced horse trader concerning the age of a horse. The same is true for other farm animals and indeed for humans. Skin, hair, eye, voice, the very movements of the body and of its parts bear witness to the passing of years, to chronological age. It is not, however, as easy to *measure quantitatively* physiologic or anatomic aging as it is to measure early growth with balance and tape.

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[57] For detailed reasons, for possible importance of increasing vitamin intake with increasing age see Ch. 6, especially the reference to Rhoads, C. P.; also Cramer, W., *Bull. New York Ac. Med.*, **17**, 3 (1941), and *Jour. Am. Med. Assoc.*, **119**, 309 (1942).

Each structure and function passes through a "prime-of-life" which joins the period of obvious growth with that of aging. Thus the *percentage growth* rate of the body as a whole is maximal or prime in the early embryonic period (Figs. 16.2, 16.17, 16.18); the *absolute growth* rate is maximal during puberty (Figs. 16.8, 16.13); the minimal specific mortality or maximal vitality (reciprocal of mortality) occurs shortly before puberty (Figs. 16.8, 18.22–3); the absolute size of the thymus (and other lymphatic tissue) occurs near puberty and rapidly declines thereafter; maximal muscular power in man occurs near age 20 years[58] (Figs. 18.14–15); maximum potential reproductive activity in man is near 20 years and declines thereafter,[59] and so on.

As previously noted, it is difficult to estimate the age of prime intellectual power because of the influence of many factors thereon. Lehman[60] estimated that the prime intellectual power in man occurs at age 30 years, but qualified this by reporting that a third of the important contributions in chemistry were made after age 40 years, a fifth after age 50 years; literary masterpieces usually appear after 45 years. However, there is always a lag between the conception of an idea and its execution on one hand and its public appearance on the other. (See also Fig. 18.15a.)

18.4: Quantitative analysis of aging data. The best quantitative measure of aging is decline in adjusting ability to emergencies (homeostasis, Ch. 10), and decline in the safety factors especially in cardio-respiratory reserve power (Sect. 24.5). The prize-fighter of 30 is likely to lose his championship to his 20-year-old rival because the reserve powers of a 30-year old are below those of a 20-year old. The greater the need for rapid adjustment (as in prize-fighting, rapid diving in airplane or submarine, undergoing violent bombardment, exposure in a life-boat in mid-ocean), the less successful the older individual (in comparison to that of a 20-year old), the more likely will he be to experience "black outs", confusional states, and many functional disorders, lumped together under the heading of "shock" and "nervous breakdown." This the Army knows, and the actual fighting in this violent, rapidly moving war is largely between youngsters.

It is rather difficult to obtain strictly quantitative data on age changes in reserve power (homeostasis), although there are likely to be such data following the war's end, as the various branches of the fighting force are working on methods for estimating such power in selectees for the services. In general, the older the individual the lower the stroke volume of the heart (completeness of emptying of the ventricle per heart beat), therefore, the higher the pulse rate for a given exertion and less efficient the circulatory process. Moreover, the older the individual the lower the ceiling for the pulse rate, so that under conditions of stress circulation cannot keep up with the needs in

[58] Lehman, H. C., "The most efficient years in sports." *Res. Quart. Am. Ass. Health and Physical Education* **9,** 3 (1938).

[59] Pearl, R., "The natural history of populations." New York, 1939.

[60] Lehman, H. C., *Sci. Monthly*, **43,** 151 (1936), **45,** 65 (1937); **59,** 384 (1944).

the old as well as in the young. The young and old are equally comfortable—maintain equal homeostasis—at rest, but not above a certain work level. Fig. 18.3b shows the age decline in cardiac reserve power (see Ch. 24 for detailed discussion of this index of cardio-respiratory reserve).

Attempts have also been made to measure reserve power in experimental animals by the ability to withstand poisons[62] and bleeding.[63] Sims[63] reported that 825-day-old rats died with 12 per cent less hemorrhage than 100-day old rats; or in terms of probabilities of death, these are 16 times as great in 825 as in 100-day old rats.

The prime of life is not a point but a zone, the width of which varies with the particular index of aging employed. Fig. 18.3a illustrates the age changes in reaction speed to an electric shock[64] in rats, dependent on the function of many integrative and conducting devices. Egg production in fowls is in its prime during the first year (Fig. 18.11), but milk production in dairy cattle is not attained until the seventh year (Fig. 18.16).

Our basic problem is to describe quantitatively, mathematically, the decline in (reserve and homeostatic) power to withstand unfavorable conditions.

It is, of course, clear that by the time an animal attains the upper limit of the species-life-span it has experienced many risks, some from the external environment (infections, etc.) and others "spontaneous" (as blood clots, erosions, etc.) which eliminated at various ages most of its fellow travellers on the life cruise. The probabilities of elimination of a given individual at a given age, on a given age curve of specific mortality depends, on at least three well-defined factors: (1) impact intensity of the injuring agent, (2) susceptibility or resistance of the individual to the injuring agent, and (3) induction period, that is, the time intervening between the initial injury and death. Thus production of fatal cancer by coal tar requires about a fourth of a lifetime (about six months in a mouse and fifteen years in man). Many, if not all, deaths associated with aging are thus terminal stages of "remote causal factors".[65] The same may be said of other cancer deaths—whether initiated by estrogens, methylcholanthrene or by the Bittner[66] factor.

Such general considerations and the fact that resistance or reserve power declines with increasing age to all injurious agencies suggests the idea that specific mortality is likely to follow an exponential course with increasing age,

[62] Cameron, J. A., "Difference in resistance to CO asphyxia," *J. Cell. and Comp. Physiol.*, **18,** 379 (1941).

[63] Simms, H. S., *Science*, **91,** 7 (1940); **95,** 183 (1942).

[64] Brody, E. B., *J. Gen. Physiol.*, **24,** 433 (1941); *Growth*, **6,** 179 (1942).

[65] Cramer, W., "The origin of cancer in man," *Jour. Am. Med. Assoc.*, **119,** 309 (1942).

[66] The following papers indicate that breast cancer in adult mice is probably associated with the infantile nursing of cancerous mothers. Incidentally, breast cancer is absent in dairy cattle but frequent in humans and mice. Bittner, J. J., "Mammary tumor incidence in mice," *Science*, **84,** 162 (1936). "Breast cancer and mother's milk," *J. Heredity*, **28,** 363 (1937); *Am. J. Cancer*, **36,** 44 (1939); *J. Nat. Cancer Inst.*, **1,** 155 (1940). "Possible methods of transmitting susceptibility to breast cancer in mice," *Am. J. Cancer*, **39,** 104 (1941). Andervont, H. H., and McEleney, W. J., "Influence of foster nursing on incidence of cancer in mice," *Public Health Repts.*, **54,** 1597 (1939) and *J. Nat. Cancer Inst.*, **1,** 147 (1940). Smith, J. L., "Growth," Edinburgh, 1932.

that is, after passing the "prime of life" when mortality is minimum. This we[67] found to be the case for the specific mortality of man as well as for the fruit fly *Drosophila*. In brief, it appears that aging may be represented quantitatively by the same exponential or mass-action, or compound interest, equation

$$Y_1 = Ae^{kt} \tag{18.1}$$

that we used for representing early growth (Ch. 16). If one prefers, the equation

$$Y_2 = Ae^{-kt} \tag{18.2}$$

may be employed to represent the course of "vitality". Y_1 represents specific mortality and Y_2 specific vitality, the reciprocal of mortality; k represents the instantaneous mortality (or vitality) rate per unit time and at age t. The "vitality equation" (18.2), in the exponent k is negative, is more convenient for representing the age course of decline in egg and milk production, and healing of wounds.

When plotted on an *arithmetic* grid the slope of the curve represented by equation (18.1) increases exponentially and that of the curve represented by equation (18.2) decreases exponentially; when plotted on an *arithlog* grid, the slope, k, is constant, rising linearly in equation (18.1) and declining linearly in equation (18.2). Let us analyze actual aging data with the aid of these equations.

18.4.1: Analyses of aging in the domestic fowl and in man. Three sets of data on aging are shown in Fig. 18.11: upper left, age changes in egg production in Leghorn fowls;[68] lower left, age changes in suitability of chicken serum as a nutrient medium for fibroblasts[69] *in vitro* cultures; right, age changes in the index of healing of wounds (cicatrization) in man.[70]

Equation (18.2) fits all three sets of data satisfactorily. The values of k are given on the chart; they are 0.12, 0.18, and 0.03, meaning that the instantaneous declines of egg production, duration of life of fibroblasts in chicken serum, and healing of wounds in man are, respectively, 12, 18, and 3 per cent per year. The rate of aging of the domestic fowl as measured by the decline of the ability of its serum to support life in fibroblasts is 6 times (= 0.18/0.03) that of man, as measured by the rate of healing of wounds. Is the potential span of life of man six times that of fowl?

The fitted equation for the egg production curve, namely,

$$Y = 179.2e^{-0.12t}$$

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[67] Brody, S., "The kinetics of senescence," *J. Gen. Physiol.*, **6**, 245 (1924); Univ. Mo. Agr. Exp. Sta. Res. Bull., 105, 1927; *Growth*, **1**, 60 (1937).

[68] Brody, S., Henderson, E. W., and Kempster, H. L., "Senescence of the domestic fowl," *J. Gen. Physiol.*, **6**, 41 (1923).

[69] Carrel, A., and Ebeling, A. H., *J. Exp. Med.*, **34**, 399 (1921). Brody, S., *J. Gen. Physiol.*, **6**, 245 (1924).

[70] du Noüy, P. L., *J. Exp. Med.*, **24**, 463 (1916). Brody, S., *J. Gen. Physiol.*, **6**, 245 (1924).

means that egg production begins at the *theoretically* maximum value of 179.2 eggs per year (that is, $Y = 179.2$ when $t = 0$), and since the decline in egg production is 12 per cent per year, the half value of A (179.2) is theoretically reached in 5.8 years; that is, $d = \frac{ln2}{k} = \frac{0.693}{0.12} = 5.8$ years (Sect. 16.3).

As previously noted, the age course of specific mortality probably reflects decreasing reserve to meet certain exigencies, such as attacks of pneumonia organisms.• Does specific mortality follow an age course similar to that of healing of wounds? It should; and it does as illustrated in Fig. 18.12 for man and in Fig. 18.13 for *Drosophila*, plotted respectively from census data compiled by Dublin[71] and from experimental results by Pearl and Parker.[72]

The specific mortality data were plotted on arithlog grids. Their linear distribution means that the age course of specific mortality follows an exponential course, as represented by equation (18.1). As before, k represents the instantaneous increase per year for man, or per day for *Drosophila*, and d is the time in years or day, respectively, in which the mortality is doubled. Thus, the value of k for deaths from pneumonia is 0.05, meaning that the specific mortality or specific probability of dying from pneumonia increases at the instantaneous rate of 5 per cent per year, that is, it increases in geometric progression, and is doubled every 7.7 years. The value of k for specific mortality from pneumonia is seen to be higher than for healing of wounds. The value of k for *Drosophila* mortality is approximately 0.4, meaning that under the given conditions the mortality increases at the instantaneous rate of 4 per cent per day, or that it is doubled approximately every 18 days.

Equation (18.1) used[67] for representing the course of aging as measured by the increase in specific mortality was recently employed by Simms[63] for the same purpose and with similar results.

The value of k for mortality from infectious diseases (such as pneumonia) is of the order of 0.05; for cardiovascular-renal diseases it is more than double this value, 0.10–.12, which means that the prevalence of circulatory diseases increases very much more rapidly with increasing age. Death from pneumonia and similar infections occurs at all ages; but of circulatory diseases (except of the infectious rheumatic-fever type) rarely below age 40 years. It takes time for the setting of the circulatory system colloids and the clogging of the system with inert material. Likewise as regards the increase in cancer mortality, which has a value of k of 0.11, in the same class with circulatory diseases (Fig. 18.12), and the development of which involves a long induction period or a loss of organismic inhibitory control over cells which become cancerous. The increase in mortality from infection and cancer is perhaps secondary to or dependent on the decline in the circulatory system, which is the regulator of the internal environment.

18.4.2: Relation between growth and aging as measured by the course of milk production and similar processes. The larger size associated with growth enables an animal to produce more milk, or to produce larger eggs, or to accomplish more muscular work, but the animal also ages during the growth process; the growth process is also a senescence process. The life course of a function, such as of milk production or muscular work, is consequently of a rising and declining pattern. The rising segment reflects the increase in body size as well as of functions during growth; the declining, the aging process at constant body size.

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[71] Dublin, L. I., "Mortality statistics of insured wage earners and their families," New York, 1919. The data represent the general population experience of males, of the expanding United States Registration Area 1910–15. See also *U. S. Bureau of the Census, Special Reports*, **5**, 303 (1936).

[72] Pearl, R., and Parker, S. L., "Experimental studies on the duration of life," *Am. Nat.*, **55**, 481 (1921).

Data are available on a number of age functions which illustrate the rising and declining pattern. Examples are vital capacity (Fig. 18.14) muscular strength (Fig. 18.15) and response to shock (Fig. 18.3a); but the most interesting agriculturally is the course of milk production, both for the life course (Fig. 18.16) and for the lactation period[73] (Figs. 18.17 and 18.25).

The rise in milk production up to seven or eight years in dairy cattle parallels in shape, although it lags in time, the rise in body weight. This is illustrated in Figs. 18.18 and 18.19. The age curve of milk production (up to 7 years) reflects the increase in size of the biological plant which produces the milk. Following age eight years, the decline in milk production reflects the aging process uncomplicated by increase in size in the milk-forming plant.

The life curve of milk production in Fig. 18.16 has this defect: the population has been rapidly decreasing with increasing age;[74] the comparison is thus made between the productive levels of animals that survive up to relatively advanced ages with others that do not survive so long. Other age curves suffer from similar defects. There is no doubt, however, that this curve illustrates the general quantitative relation between growth and senescence (Fig. 18.35 represents the age curves of the same individuals).

More spectacular in some respects than the life curve of lactation (Fig. 18.16) is the lactation-period curve of lactation, part of which is shown in Fig. 18.17. Here is an illustration of a cyclic, reversible, senescence process. Normally each year the mammary gland of dairy cattle comes to life functionally and, in many respects, structurally, and declines.

Not only the mammary gland but many other parts normally go through an annual rejuvenating and senescence process. During the lactation period the cow is in negative balance with respect to many substances. The losses are regained during the rest period.

The annual rejuvenation of the cow's mammary apparatus recalls a picture of Child's planarians (Fig. 18.20) which revert to the immature form on starvation. (See comments on McCay's retardation experiments.)

Returning to the aging of the lactation function, it appears that the decline in milk production following the attainment of the maximum yield at the prime of life or the prime of the lactation period is exponential, as indicated by equation (18.2). This is illustrated in Fig. 18.21, showing the decline in milk yield with the advance of the lactation period in a series of dairy cattle and dairy goats.[75] The lines represent the fit of equation (18.2) to the data.

The breaks in some curves with the resulting B segments reflect the fact that the animals were bred early in the lactation period and were performing a dual function, lactation and gestation. The difference between lines A extrapolated and B represents the depressing influence of gestation on lactation.

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[73] Based on Missouri Res. Bull., 105 in which the history of this problem is presented in detail.

[74] See Missouri Res. Bull. 96 for the original data, and number of animals for each age. See Fig. 18.37 for the age course of survivors in dairy cattle populations.

[75] Brody, S., Mrs. Carl Sandburg and S. A. Asdell, Univ. Missouri Agr. Exp. Sta. Res. Bull., 291, 1938.

The values of the exponents represent the instantaneous declines in milk production per month. Thus the equation $Y = 45.3\ e^{-.055t}$ represents the fact that milk yield declines at the instantaneous rate of 5.5 per cent per month; or what is the same, the instantaneous *persistency* of milk production is $100 - 5.5 = 94.5$ per cent per month—each month's yield is 94.5 per cent of the preceding month's yield.

Note that the value of the exponent, k, for curve 6 is 0.17; for curve 1, 0.053. This means that the rate of aging of the lactation function in cow 6 is about three times that in cow 1. Obviously, these curves represent the aging of a special structure-function, not of the body as a whole, because cow 6 could not be aging three times as rapidly as cow 1. Different structures in the body age at different rates.

Fig. 18.21 represents the declining segment of the lactation curve. Fig. 18.17 represents the rising phase and its relation to the declining phase.

An interesting feature in Fig. 18.17 is that the rising segment of the curve resembles the segment of the growth curve following the major inflection (Ch. 16), and that it may be represented by the growth equation employed in Chapter 16 for representing that phase, namely (see Fig. 18.25)

$$Y = A - Be^{-kt} \tag{18.3}$$

This equation was combined with equation (18.2) to obtain

$$Y = Ce^{-k_1t} - De^{-k_2t} \tag{18.4}$$

Equation (18.4) has the *form* of the expression employed by physical chemists for representing simultaneous consecutive reactions of the first order, and no doubt simultaneous consecutive processes do take place. But in view of the complicated nature of lactation, it would be naive oversimplification to say that the processes are limited by two consecutive chemical reactions, although the concept of "master reaction" could permit one to say that the course of lactation may be limited by two relatively simple factors, one of which rises initially, representing the building up or growth phase, while the other declines, representing the aging or the senescence phase. We might interpret these age changes by referring to the changes in number and activity of the secreting cells and/or to changes in ovarian and pituitary activities. But for the present purposes it seems best to present the relationships between milk flow and time as frankly empirical equations in familiar *form*.

Equation form (18.4), representing the age course and the lactation-period course of milk production, may also be rationally employed for representing the age course of "vitality" defined by the reciprocal of specific mortality. The homeostatic mechanisms are weak during infancy and early childhood, attaining a maximum by puberty, then declining. One may, therefore, say that "vitality" increases during growth and declines during aging, as reflected by the reciprocal of specific mortality with increasing age. Figs. 18.22 and

18.23 reproduce our early attempt to fit equation (18.4) to the reciprocals of specific mortality data. Fig. 18.24 represents the fit of equation (18.4) to data on basal-metabolism per square meter of surface. Additional age curves for metabolism are given in Figs. 18.5 to 18.8.

Both growth and aging tend to follow an exponential course (Sect. 16.4). The central feature of an exponential course is constant *percentage* change. The change may be positive, exemplified by accumulation at compound interest; it may be negative, exemplified by depreciation at constant percentage. Some criteria of aging, such as decline in egg production, exemplify the constant-percentage depreciation concept [equation (18.2)]; others, *e.g.*, increase in specific mortality or early growth, exemplify the constant-percentage growth concept [equation (18.3)]; others, such as the increase in milk production in cattle from 2 to 7 years, exemplify cumulative increase at decreasing constant percentage rate, reflecting the later phase of growth; still others exemplify a summation of two types of change [equation (18.4) and Fig. 18.16 and 18.17].

18.5: Summary and appendix. A critical examination of the aging problem confirms Minot's generalization that aging is associated with cessation of growth, or rather decline in growth rate, since the body is in a dynamic state[76] and repair is a continuous process, so that the replacement type of growth continues until the end of life. Prolongation of the period of growth is thus likely to be associated with prolongation of the life span, with the prolongation of the mean persistence of a cell or tissue. This may explain the greater longevity of the late-maturing species and perhaps of some individuals within a species, as those of McCay's rats that survived a protracted period of retarded growth.

It is assumed that the body tissues, which are colloids, set and age in the general manner of inorganic colloids or of protein *in vitro*, although the details are different because of the dynamic nature of the tissue. According to this assumption, the rate of aging may be controlled, within limits, by prolonging the growth period, by avoiding high levels of metabolic activity and toxic influences, and by keeping the colloidal structure sound by proper diet. The extent of such control depends on the species. Some bacteria may be kept alive very long by low temperature (which depresses the metabolism). This method applies, within narrower temperature limits, to insects and other cold-blooded animals and to warm-blooded hibernators. Low temperature has the opposite, or metabolism-stimulating effect on warm-blooded, non-hibernating animals. The same is true of the prolongation of the growth period (that is, maintenance of new tissue). The life of a flat worm (planarian) was increased twenty-fold by compelling it to produce new tissue as result of periodic starvation and realimentation, and of an amoeba as result of periodic removal of a part of its body. The maximum life span of rats has been extended by growth retardation, by caloric (but not vitamin, mineral, or protein) undernutrition. These methods may not, however, be practical for prolonging the average life span because even caloric undernutrition reduces general vitality (in part by encroaching on the body protein which is used as fuel) so that only the few escaping death by the retardation process are benefited. The remedy may be worse, for most individuals, than the disease. This method is, of course, inapplicable to farm animals kept for high productive levels involving high metabolic rates.

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[76] Schoenheimer, R., "Dynamic state of body constituents," 1942.

Charts and mathematical equations, so-called "laws", are presented for the time relations of aging in man, fruit fly, fowl, and dairy cow. The central mathematical feature of the aging process following the prime of life is that it tends to be exponential; that mortality probabilities, for example, increase in a geometric ratio, according to the "mass law". Thus while the specific mortality in an adolescent human is about one in 800—a mortality rate which if continued through life would give a life expectancy of 600 years—the mortality rises (beginning with puberty) exponentially with increasing age at the rate of about 11 per cent per year for the degenerative diseases, such as vascular diseases and cancer, and at about 5 per cent for infectious diseases, so that the actual expectation of life is nearer 60 than 600 years.

A notable feature of *some* of these aging curves is that their slopes are, within limits, under control. Thus the average human life span has been rapidly increasing by better control of infections, diet, work and other conditions discussed in the text. Thus the mean life expectancy at birth in the United States was 36 years in 1800, 40 years in 1850, 50 years in 1900, 55 years in 1920, 60 years in 1930, and 64 years today. The average expectation of life at birth in Western Europe has increased from 20 years in the 16th century to 25 years in the 17th century, 32 years in the 18th century, 40 years in the 19th century, 49 years in 1900, 59 years in 1925, and near 62 years in 1938.

While, however, more people live to be old, the maximum life span has not been increased. Aging and death are the most certain characteristics of life, characteristics not without their advantages:

> "In a world of great complexity, the attention of man is turned with relief to the more determinate limits of life. . . . The very definiteness of such points heightens the sense of reality. Death in particular is characterized by a finality which seems decisive. But death is only the end point in a long chain of events, and biologically it may be best understood in terms of the antecedent physicochemical processes.[77]

The following numerical illustration of the equations and charts is presented for readers who feel more at home with original numerical values than with generalizing equations and curves.

The first table is a compilation of basal metabolism data at various ages obtained on "professors" and other persons well known to students of metabolism, and this table is, therefore, likely to have a personal interest to many readers beyond theoretical implications.

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[77] Cohn, A. E., and Murray, H. A. Jr., "Physiological ontogeny," *Quart. Rev. Biol.*, **2**, 469 (1927).

Basal Metabolism of "Professors" and Other Well-Known Persons

"Professor"	Ages (years)	Basal metabolism, Cal. per 24 hours per			Weight (kg)	Height (cm)	Pulse per min
		person	sq. meter	kg			
Magnus-Levy[78]	26	1608	914	23.8	68	167	50 (?)
	76	1248	756	20.9	60	165.5	40
Zuntz[79]	41	—	804	17.3	66	—	—
	63	—	792	16.8	69	—	—
	70	—	725	15.9	59	—	—
Lusk[80]	44	1970	1027	25.9	76	175.6	—
	58	1522	785	19.5	78	—	—
Benedict[81]	38	1837	900	22.1	83	183	68
	48	1600	800	20.4	80	"	60
	58	1563	785	20.4	77	"	56
Du Bois[80,78]	30	1862	974	25.2	74	178.5	—
	41	1700	881	22.7	75	"	—
	58	—	828	—	—	—	—
Carpenter[81]	31	1367	896	27.8	49	655	73
	42	1181	782	24.6	48	"	65
	49	1070	695	21.4	50	"	64
H. M. Smith[81]	43	1334	758	22.6	59	181	55
	48	1383	777	22.8	61	"	64
	59	1376	760	22.0	63	"	70
Miss W	24.5	1302	824	23.0	57	161	64
	30.5	1376	844	22.8	61	"	62
	34.5	1258	772	21.0	60	"	48

The following table, averaged from Lewis,[82] represents averages of about ten different persons for each age class (see also Figs. 18.5 and 18.6).

Age (years)	Cal. per 24 hours per:			Weight (kg)	Height (cm)
	person	sq. meter	kg		
40–44	1624	893	23.3	70.7	172.4
45–49	1561	854	23.1	65.4	174.4
50–54	1535	864	23.1	67.4	171.2
55–59	1469	790	20.4	72.3	175.0
60–64	1485	826	21.8	69.1	172.1
65–69	1542	871	23.5	66.9	171.1
70–74	1441	826	21.8	70.0	167.2
75–79	1459	826	21.2	68.9	167.1
80–84	1386	809	22.1	63.2	167.7
85–89	1314	802	23.2	57.0	166.2
90–101	1207	715	20.4	60.0	170.6

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[78] Magnus-Levy, A., *J. A. M. A.*, **118**, 1369 (1942).

[79] Zuntz, N., und Loewy, A., *Berl. Klin. Wochnschr.*, **53**, 825 (1916), and *Bioc. Z.*, **90**, 244 (1918).

[80] Lusk, G., and Du Bois, E. F., *J. Physiol.*, **59**, 213 (1924).

[81] Benedict, F. G., *Am. J. Physiol.*, **85**, 650 (1928).

[82] Lewis, W. H., Jr., *Am. J. Physiol.*, **121**, 502 (1938).

The following basal metabolism values on Japanese are from Kise & Ochin[83] (converted by the author to a 24-hour basis).

Age (years)	Basal metabolism Cal/sq. meter/day	
	Men	Women
20–50	895	811
50–59	865	816
60–69	838	796
70–79	796	766
80+	769	730

The following *smoothed* basal metabolism "standards" are from Boothby[84] and associates (converted to a 24-hour basis by the author).

Age (years)	Basal metabolism Cal/sq. meter/day	
	Male	Female
6	1278	1217
8	1245	1102
10	1160	1102
12	1127	1056
14	1117	1009
16	1106	950
18	1079	896
20	1020	882
25	980	866
30	960	848
40	911	849
50	885	814
60	845	832

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[83] Kise, Y., and Ochin, T., *J. Lab. and Clin. Med.*, **19,** 1073 (1934).

[84] Boothby, W. M., Berkson, J., and Dunn, H. L., *Am. J. Physiol.*, **116,** 468 (1936).

The following set of metabolic data on individual old women (and five men) is the most complete available and indicates the order of variability and apparent lack of correlation between metabolism, pulse rate, vigor, and other physiologic "constants". Compiled from Benedict, F. G., and Meyer, M. H., *Am. Phil. Soc.*, **71**, 143 (1932), and *New Engl. J. Med.*, **212**, 1111 (1935). See also Fig. 18.3b.

Age (years)	Heat production, Cal/24 hrs.			Pulse rate	Blood pressure, mm.		Weight (kg)	Height (cm)	"Vigor"
	per sq. meter	per kg.	total		Systolic	Diastolic			
66	621	19	931	63	154	84	50	159	A
68	800	19	1359	72	194	102	71	154	C
70	810	19	1401	75	178	110	72	157	B
70	762	21	1112	80	230	120	52	150	C
71	858	21	1501	80	170	90	72	159	C
71	714	18	1140	72	160	100	64	153	B
71	752	20	1323	69	182	120	67	168	B
71	726	21	1096	71	210	110	53	156	A
73	799	21	1318	58	170	85	64	157	C
74	715	18	1122	76	194	100	63	149	C
74	654	21	936	65	170	90	45	159	A
76	803	23	1148	68	182	82	49	152	B
77	713	25	799	60	172	84	32	138	A+
78	749	23	973	65	150	100	42	145	C
79	636	15	1049	70	160	100	69	151	C
81	723	24	961	72	180	130	41	152	A
81	647	16	1035	56	160	80	67	147	A+
84	720	20	1015	64	170	90	50	146	A
84	741	24	1045	74	200	70	44	158	B
84	811	24	1070	74	150	90	45	144	C
84	705	21	973	67	180	120	45	151	A
84	619	15	966	73	164	100	63	147	E
86	693	19	1026	78	142	64	54	150	A
69	709	21	1042	67			50	156	B−
72	815	19	1549	64			81	167	C
72	680	22	966	55			44	160	C
73	649	17	1077	63			62	162	B
75	813	23	1292	56			55	164	B
75	744	19	1265	56			68	159	B+
79	727	25	938	71			38	153	B−
80	805	20	1223	55			62	144	A
86	676	22	980	55			44	164	B
88	630	18	938	57			53	153	D
				and 5 old men					
74	776	20	1466	48			74	175	A
74	730	20	1271	54			65	168	C
82	866	22	1688	36			79	176	D
87	796	22	1362	50			63	167	C
87	572	17	910	44			52	164	A

The following table represents the age changes in blood pressure in man [after Master, Marks, and Dock, *J. A. M. A.*, **121**, 1251 (1943)].

Percentage Hypertension at Ages on Top Row

Age	40–49		50–59		60–69		70–79		80–89		90–99	
Blood pressure (mm)	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
140/90 or over	33.6	39.2	49.2	64.8	66.5	77.9	77.1	81.7	77.7	84.7	87.0	81.1
150/90 or over	25.9	32.0	40.6	53.4	56.3	67.7	65.5	73.3	66.5	76.6	78.3	73.3
150/95 or over	16.9	23.6	32.8	46.6	51.0	64.5	61.8	70.2	63.3	74.3	73.9	70.3
150/100 or over	15.4	22.7	31.7	45.5	50.4	64.0	61.3	69.5	63.3	74.3	73.9	70.3

The apparent average blood pressure values for each age vary with the methods employed and with the thickness of the arm measured. Saller's data indicate relatively higher values than those usually employed by insurance companies.

Saller, K. Z. ges. exp. Med. 58, 683 (1928)			U. S. Insurance Company Standards	
Age (yrs.)	Blood pressure, mm		Age (yrs.)	Blood pressure, mm
	Males	Females		
21–35	144/98	138/99	20	120/79
35–47	154/96	155/100	30	122/81
48–53	154/97	190/100	40	125/83
54–59	159/97	196/104	50	129/85
60–67	173/93	216/102	60	135/87
65–69	186/86	222/112		

Illustration of the decline in egg production and in bird population with increasing age of domestic fowls, actual data. In the equations fitted to these data Y represents yearly egg productions (from Nov. 1 to Nov. 1) for age in years, t. Thus for the first equation the egg production began at the theoretical rate of 179 eggs and declined at the differential rate of 12% per year.

Age (years) Nov. 1 to Nov. 1	Light breed[68] (S.C.W.L.)			Light breed[85] (S.C.W.L.)			Heavy breeds[85] (B.P.R., R.I.R., & W.W.)			Av. of the same 450 S.C.W.L. birds	
	No. birds	Eggs per yr.	% of 1st yr.	No. birds	Eggs per yr.	% of 1st yr.	No. birds	Eggs per yr.	% of 1st yr.	Eggs per yr.	% of 1st yr.
1	222	158	100	1867	169	100	372	192	100	157	100
2	"	140	89	"	146	86	"	138	72	141	90
3	"	124	78	"	124	77	132	110	57	130	83
4	"	110	70	957	109	64	42	91	48	118	75
5	193	95	60	450	95	57	14	85	44	97	62
6	28	89	56	232	86	51	7	64	33		
7	27	71	45	152	66	39					
8	6	63	40	80	67	40					
9				48	51	30					
10				23	41	24					
11				5	46	27					
	$Y = 179e^{-0.12}$			$Y = 193e^{-0.14}$						$Y = 172e^{-0.09}$	

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[85] Hall, G. O., and Marble, D. R., *Poultry Sci.*, **10**, 194 (1931).

Usually the higher the egg production during the first year the lower the life span, or the lowest first year production goes with longest life and highest life-time production, as indicated by the following data[85] on S.C.W.L. birds. The equation relating egg production, Y, with life span, t, is $Y = 179e^{0.025t}$

Egg production, first year	169	160	158	156	152	145	142	141	118
Average life span, years	3	4	5	6	7	8	9	10	11
Number birds surviving	1867	957	450	232	152	80	48	23	5

The egg production in one group of fowls is given by the equation

$$E = 179e^{-.12t}$$

which means that the egg production begins at a level of about 179 eggs per year, and declines at the instantaneous rate of about 12% per year. This equation may be employed for evaluating the potential or limiting number of eggs a fowl can produce by integrating the equation between age one-half year when egg laying begins and infinity:

$$E = \int_{\frac{1}{2}}^{\infty} Ae^{-kt}\,dt = \frac{A}{K}\,[e^{-kt}]_{\frac{1}{2}}^{\infty} = \frac{179}{0.12}\,e^{-\frac{0.12}{2}} = 1370$$

It thus seems that if egg laying were to continue indefinitely, the total number of eggs laid by the average fowl of the group would be 1370, less than the number of oocytes in the fowl. It, therefore, appears that it is not the number of oocytes in the hen that limits the course of egg production, but the aging of some limiting organ or organs.

Similarly the limiting value for milk production during the declining phase of a lactation cycle is given by integration of the equation:

$$Y = Ae^{-kt}.$$

Integrating between zero and infinity, yields the ratio $\frac{A}{K}$, in which A is the initial level of milk production, and k is the differential decline of production per month. In case of the farrow group of cows in Fig. 18.21, $k = 0.055$; $A = 1170$ pounds milk per month. Hence, the limiting milk yield for a lactation period is $\frac{1170}{.055} = 21{,}300$ pounds, which is a little over twice the milk yield for the first year, about 10,000 pounds.

The above train of reasoning was used for deducting[86] several important relations, for example the ratio of milk yield during a lactation period to the initial lactation level, A, and to the decline in productivity, k, with the advancing period of lactation.

Because of the voluminous body of data on milk yield (of the 25.5 million dairy cows in the U. S. A. the milk records of ¾ million per year are made publicly available by courtesy of the breed associations and Dairy Herd Improvement Associations) and enormous differences in the absolute level of production, it is customary to present the age-change data in terms of age changes in the factors required for converting the milk yield at any age to the mature equivalent at 6 to 8 years as indicated by the following values based on a recent compilation of Dairy Herd Improvement Association data by the U.S.D.A., B.D.I., and State Agr. Exp. Stations.

Age at freshening, yr.	2–	2½–	3–	3½–	4–	4½–	5–	6–	7–	8–
Factor for converting to mature equivalent	1.29	1.21	1.15	1.10	1.06	1.04	1.01	1.00	1.00	1.02

Age of freshening, yr.	9–	10–	11–	12–	13–	14–	15–	16–
Factor for converting to mature equivalent	1.03	1.05	1.08	1.10	1.12	1.15	1.17	1.20

In other words, a 2-year animal produces about 29% below that of a mature (6 to 8 years) animal. Actually, individuals differ in their rate of change with age, and conditions of management (feed supply, frequency of milking, etc.) influence these values enormously (Figs. 18.31 to 18.35). Many tables on milk production as functions of age and of stage of lactation are given in Missouri Res. Bulletin 96.

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[86] Univ. Mo. Agr. Exp. Sta. Res. Bull., 105, pp. 48–51.

Chapter 19

Physiologic Time and Equivalence of Age

For a being to exist is to change. *Henri Bergson*[1] (philosopher)

True age depends on progressive changes of the tissues . . . some remain young for many years . . . others wear out early in life. *Alexis Carrel*[2] (physiologist)

What am I to be tonight—90 or 40? Time is merely an accommodation to me. *Ethel Barrymore* (actress)

19.1: Physical versus physiological clocks. Physical time is measured by clocks in the manner that space is measured by rods. Both are empirical or arbitrary: the meter is the distance between two marks on a standard platinum-iridium bar; the day is the time taken by the hand of a standard clock to move a given distance on its dial. The meter is supposed to represent a certain distance on the earth; the clock mechanism is adjusted so that its hands match the rate of diurnal motion of the earth around its axis. Time is thus not a "cause" of change, but a frame of reference for change. Time does not change us but we change in time. "Time is the stream I go fishing in" (H. D. Thoreau).

Physical time, measured by the rotation of the earth around its axis, is *assumed* to flow uniformly just as the standard meter stick is assumed to maintain a constant length. There is no satisfactory method for checking these assumptions.

Physiologic time, measured by the *rate of change in the organism*, is, on the contrary, variable. If the life span is 90 days in *Drosophila* and 90 years in *Homo*, we may say that the physiologic clock of the fly runs about 365 times as rapidly as that of man. Similarly, different individuals of the same species and different tissues in the same individual change at different rates, that is, have different physiologic time or age scales. This concept is generally recognized as indicated by such expressions as[3] dental age (age of appearance of permanent teeth), anatomic age (age of ossification of the carpals and epiphyses), developmental age, mental age, pedagogic age, social age, and so on. Other indices of aging may be employed as age changes in the rates of: visual accommodation, chronaxy (response to nervous stimuli), oxygen consumption (metabolism), healing of wounds, growth of tissue *in vitro* in blood serum from different individuals, nutritional processes (digestion, assimilation, excretion), mortality (changes in ability to withstand a "dose" of an unfavorable condition ranging from an attack of "cold" to removal of a given percentage of blood), milk production, egg production, muscular work, forgetting, learning, and so on.

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[1] Bergson, H., "Creative Evolution," 1906.

[2] Carrel, A., and du Noüy, P. L., "On healing of wounds," *J. Exp. Med.*, **24**, 451 and 461, (1916); **25**, 721 (1917); **29**, 392 (1919); Carrel, Ebeling, A. H., *et al.*, "Age and multiplication of fibroblasts," *Id.*, **34**, 599 (1921), **35**, 657 (1922). Carrel, A., "Physiological time," *Science*, **74**, 618 (1931); "The new cytology," *Id.*, **73**, 297 (1931); "Man the unknown," Harpers, New York, 1935.

[3] For "pubertal age" (appearance of pubic hair) see W. C. Crampton, *Am. Phys. Educ. Rev.*, **13**, 144 and 268 (1908); B. T. Baldwin, U. S. Bur. Ed. Bull., 10, 1914; Suttleworth, F. K., "Sexual maturation and growth in girls," Monographs of the *Soc. Res.*

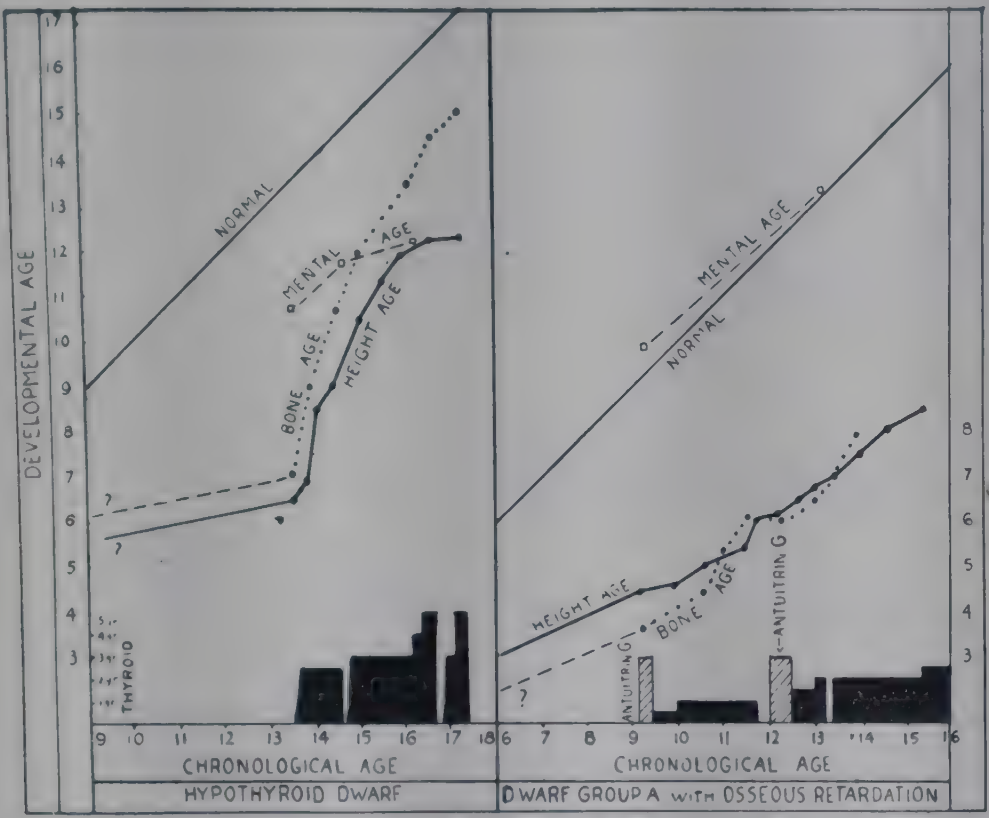

Fig. 19.1. An illustration of the use of several types of physiological ages (mental age, bone age, height age, developmental age, chronological age) for describing the growth of hypothyroid children, and of the influence of thyroid and of pituitary-extract administration on these ages. From L. Wilkins, W. Fleischmann, and W. Black, *J. Clinical Endocrinology*, **1**, No. 1, p. 3 (1941) published by C. C. Thomas, Springfield, Illinois.

The physiologic time scale changes wth age, with the amount of "personal history" lived, or with the number of physiologic events packed in a day. To the rapidly changing child a year is a long time, to the "fossilized" adult, it is a short time. To quote Carrel:[4]

Child Development, **2**, (1937), and **3**, (1938). For social and developmental age as judged by play preferences, reaction to authority, etc., see R. A. Furfey, Educ. Res. Bull., 2, 1925, Catholic Educ. Press. Washington, D. C. For evaluation of aging in man after age 25 years see T. W. Todd, *Science*, **82**, 181 (1935) (by the rarefactions in the skeleton observed by transillumination of the shoulder blades).

[4] Carrel [3], 1935.

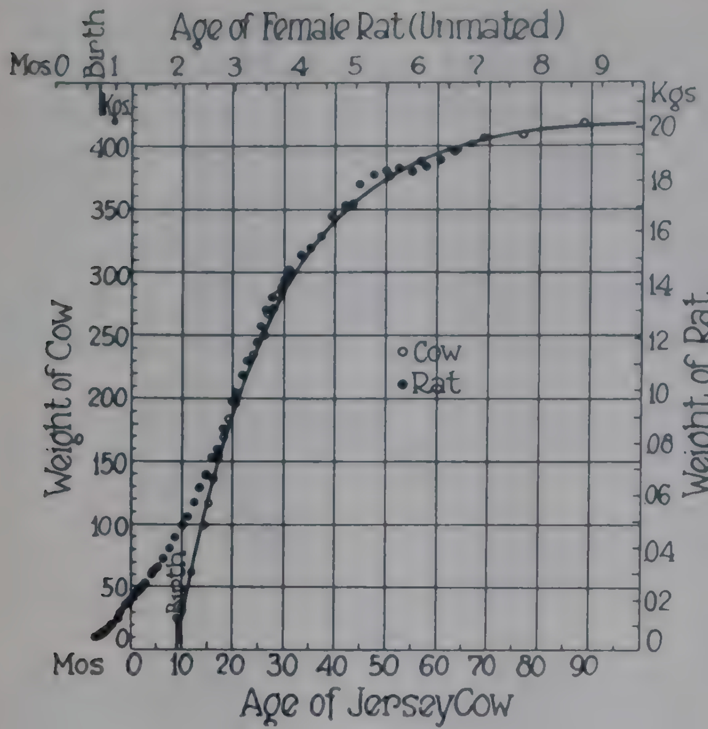

Fig. 19.2. Growth-equivalence of Jersey cow (Eckles) and unmated female white rat (Donaldson). After age t^*, 1 month in the rat is equivalent to 11.9 months in the cow, and 1 gm. of weight in the rat is equivalent to 2.068 kilos in the cow. The period of growth prepreceding the inflection is relatively longer in the rat than in the cow. (See Table 16.1 for values of k and t^*.)

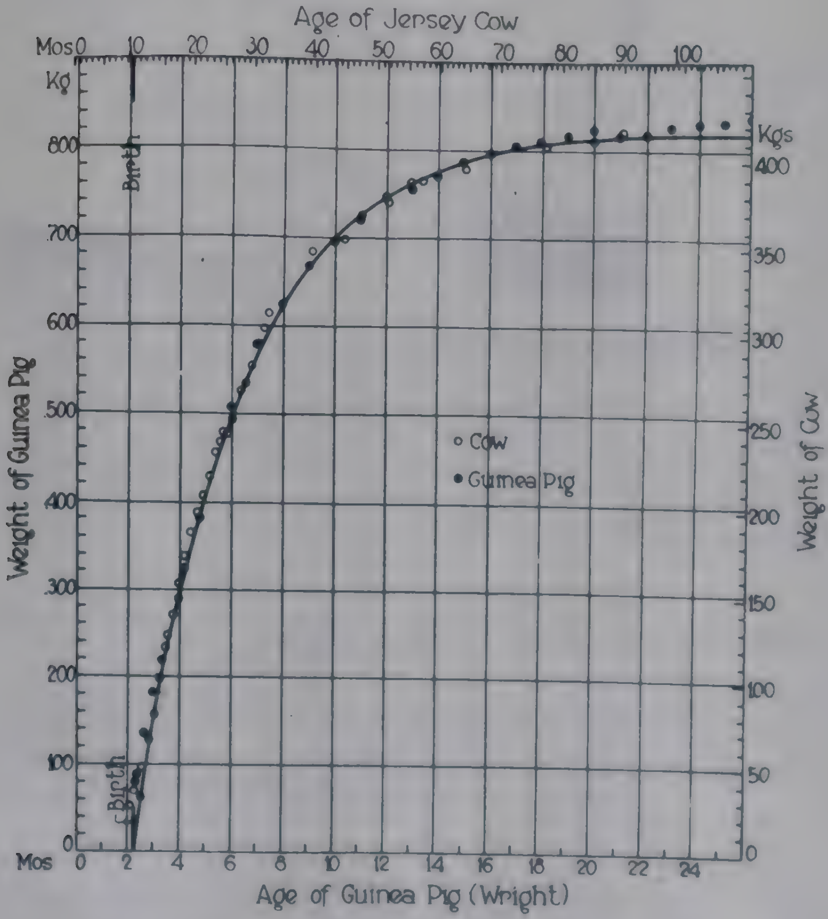

Fig. 19.3. Growth-equivalence of cow (Eckles) and guinea pig (Wright). One month in the guinea pig is equivalent to 4.26 months in the cow and 1 gm. in the guinea pig is equivalent to 509.1 gm. in the cow. Unlike in the rat, growth in the guinea pig appears to follow the same course as growth in the cow from conception.

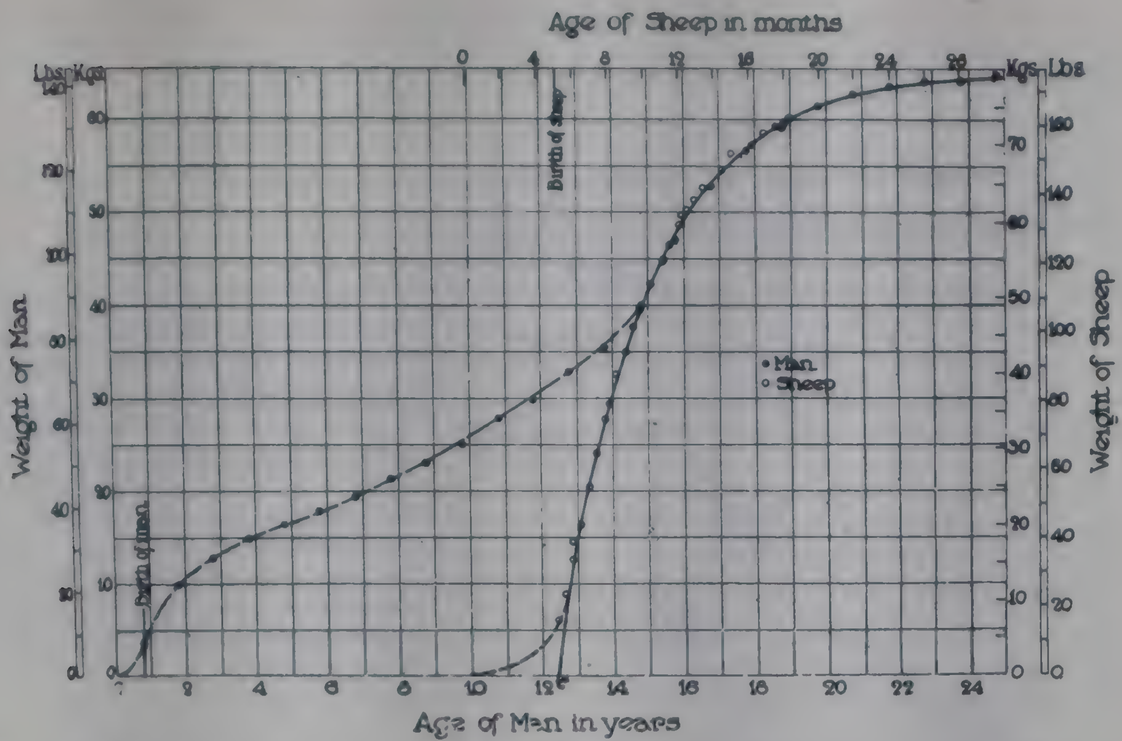

Fig. 19.4. Growth equivalence (following the major inflection) in man and sheep (of approximately the same mature weight, A). Man and sheep follow the same negatively exponential course following puberty, but the sheep is virtually devoid of the juvenile growth segment which is so characteristic of man. See also Fig. 16.7.

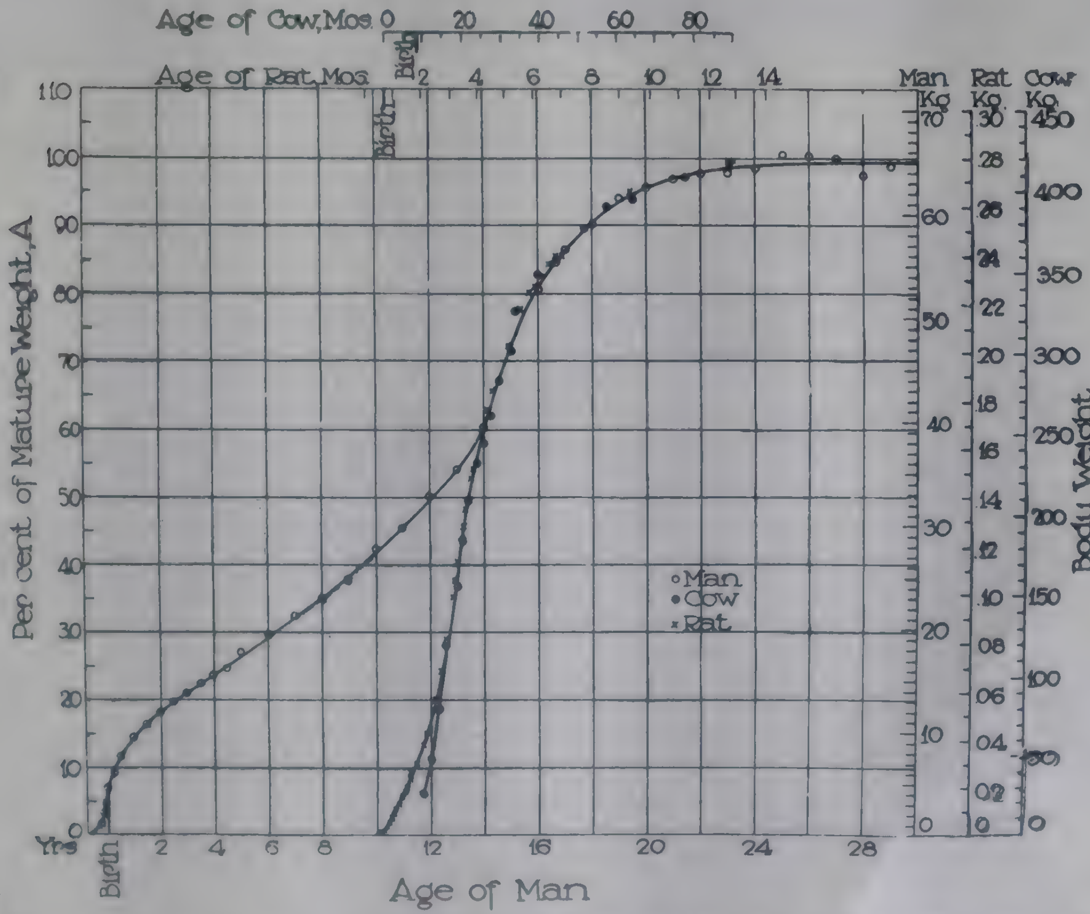

Fig. 19.5. Growth equivalence between man, white rat, and Jersey cow. The rat has a relatively somewhat longer juvenile and infantile period than the cow, and man has a very much longer juvenile period than either rat or cow. See Figs. 16.7 and 19.4.

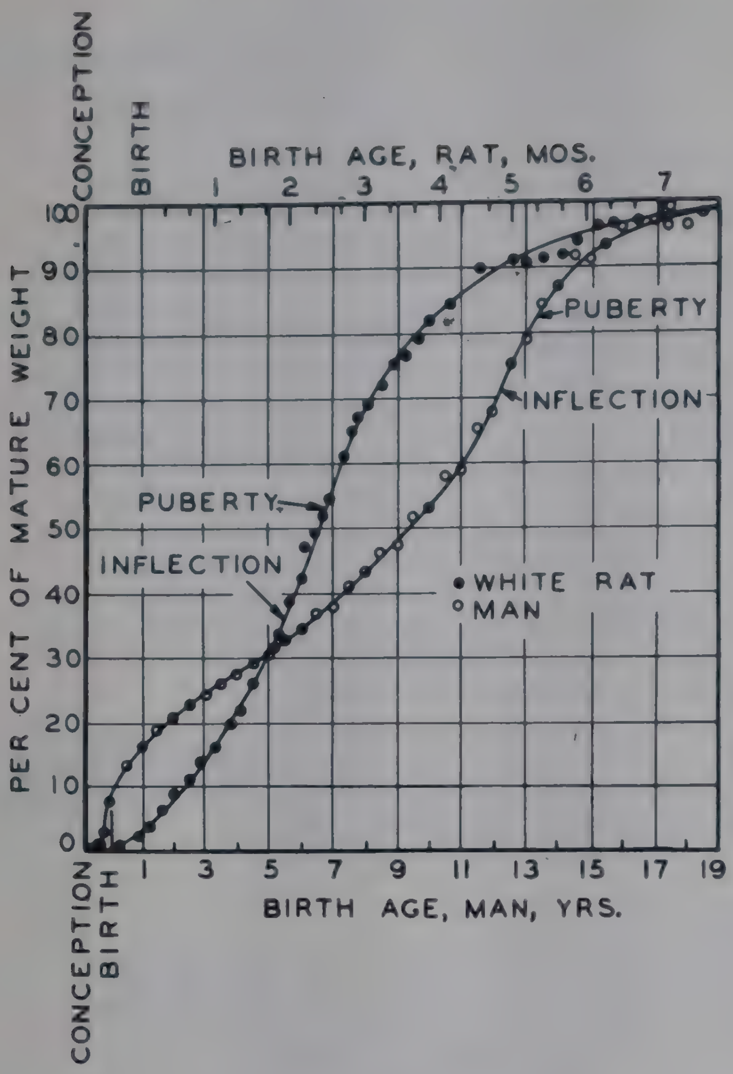

Fig. 19.6. Equivalence curve for rat and man based on the assumption that the course of growth between conception and "maturity" (when body weight attains 98 per cent of the mature weight, A) is the same in the two species. This assumption is obviously not in harmony with the facts, and this method is, therefore, not applicable for estimating equivalence of physiological age between man and other species.

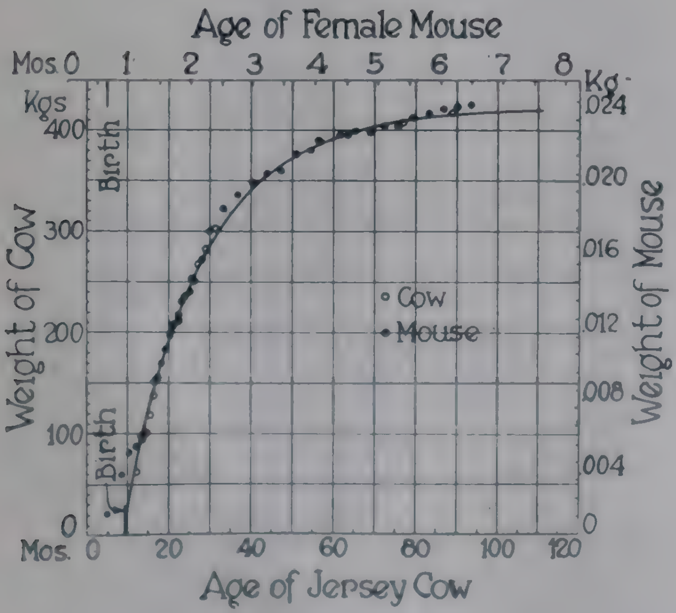

Fig. 19.7. Growth equivalence (following t^*) of Jersey cow and female white mouse. One month in the mouse is equivalent to 15.29 months in the cow. The segment preceding t is longer in the mouse than in the cow.

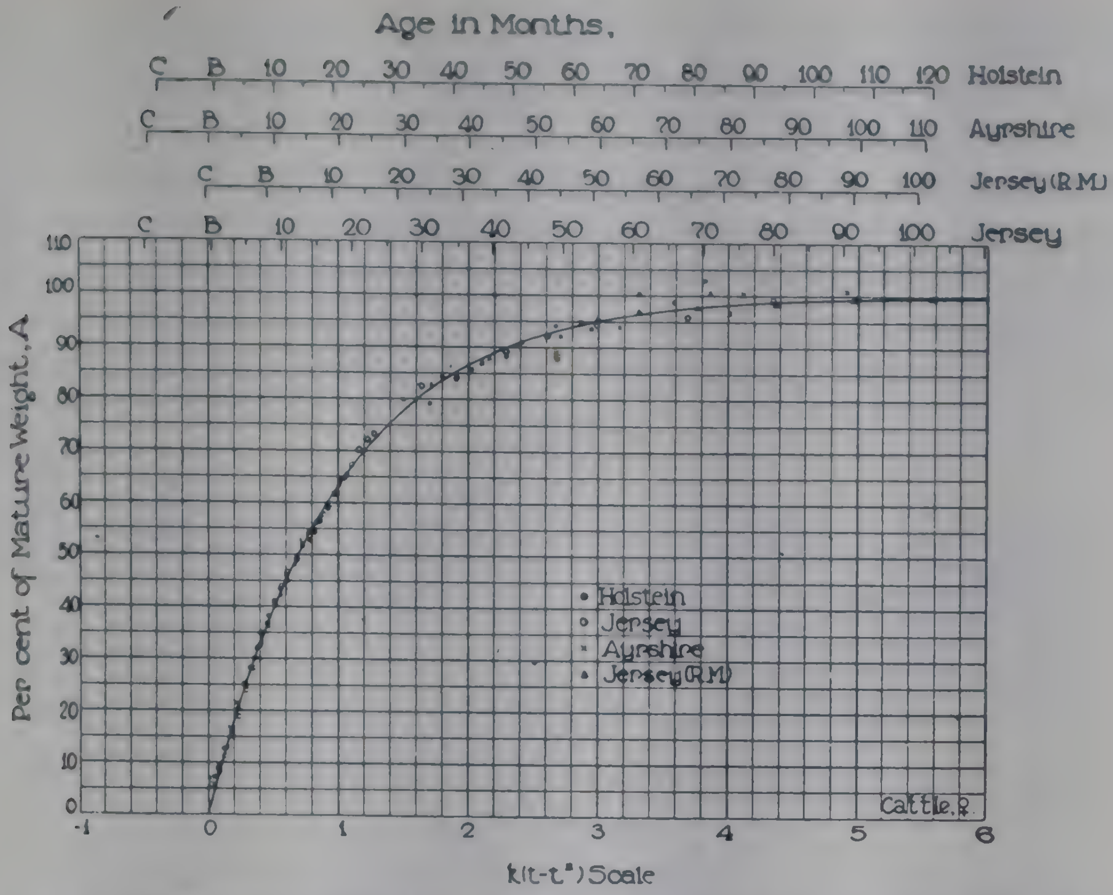

Fig. 19.8. Growth-equivalence for three breeds of dairy cattle plotted on the equivalent-time scale $k(t - t^*)$. C represents conception and B, birth. See Table 16.1 for the numerical values of k and t^*.

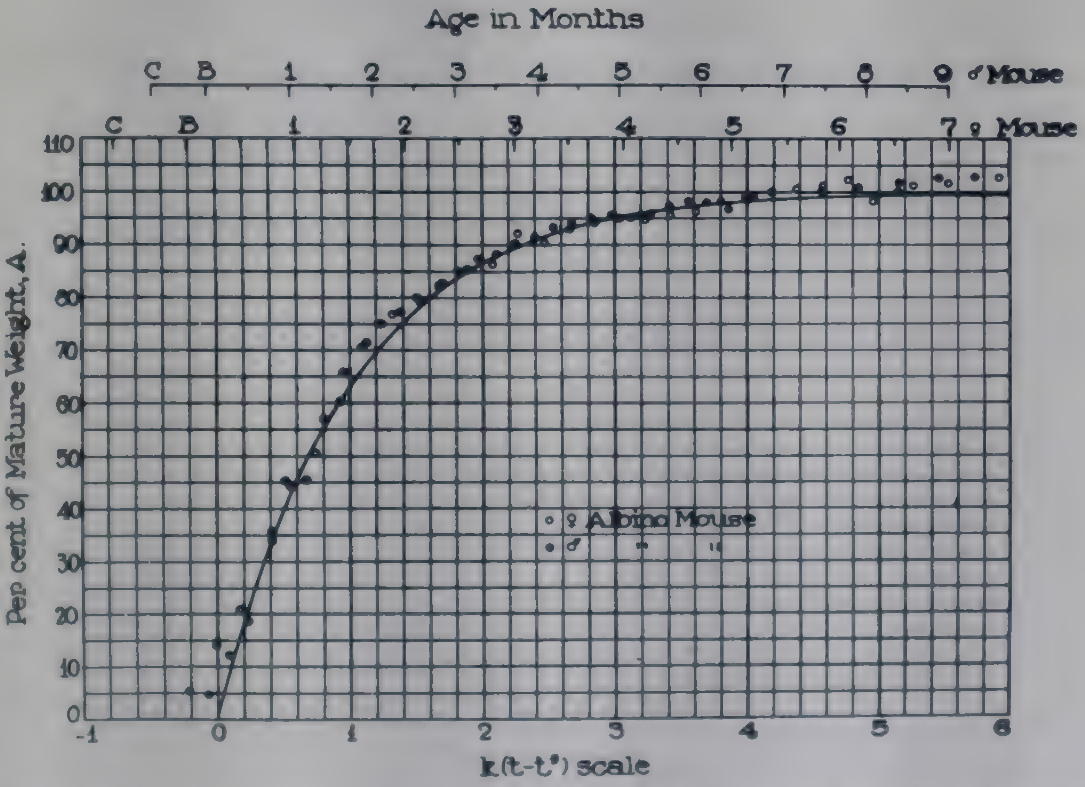

Fig. 19.9. Growth equivalence for male and female white mice plotted on the equivalent-time grid $(k(t - t^*)$.

> The content of a year in units of physiological time . . . is different for each period of an individual's life. . . . At the dawn of his life, man briskly runs . . . faster than the stream. . . . Toward midday, his pace slackens, the waters now glide as he walks. When night falls . . . man drops far behind. Then he stops . . . and the river continues on.

Anything which accelerates the rate of living accelerates the physiological-time clock so that, by comparison, the physical time clock appears to be retarded. Thus when body temperature is increased by fever, spontaneous[5] or induced,[6] time seems to pass more slowly because the body clock runs faster by comparison. The estimation of the flow of time (*e.g.*, counting 60 at the rate believed to be 1 per second and recording the time by a stopwatch), when plotted against body temperature, gives a slope in agreement with the van't Hoff-Arrhenius equation (Ch. 11).

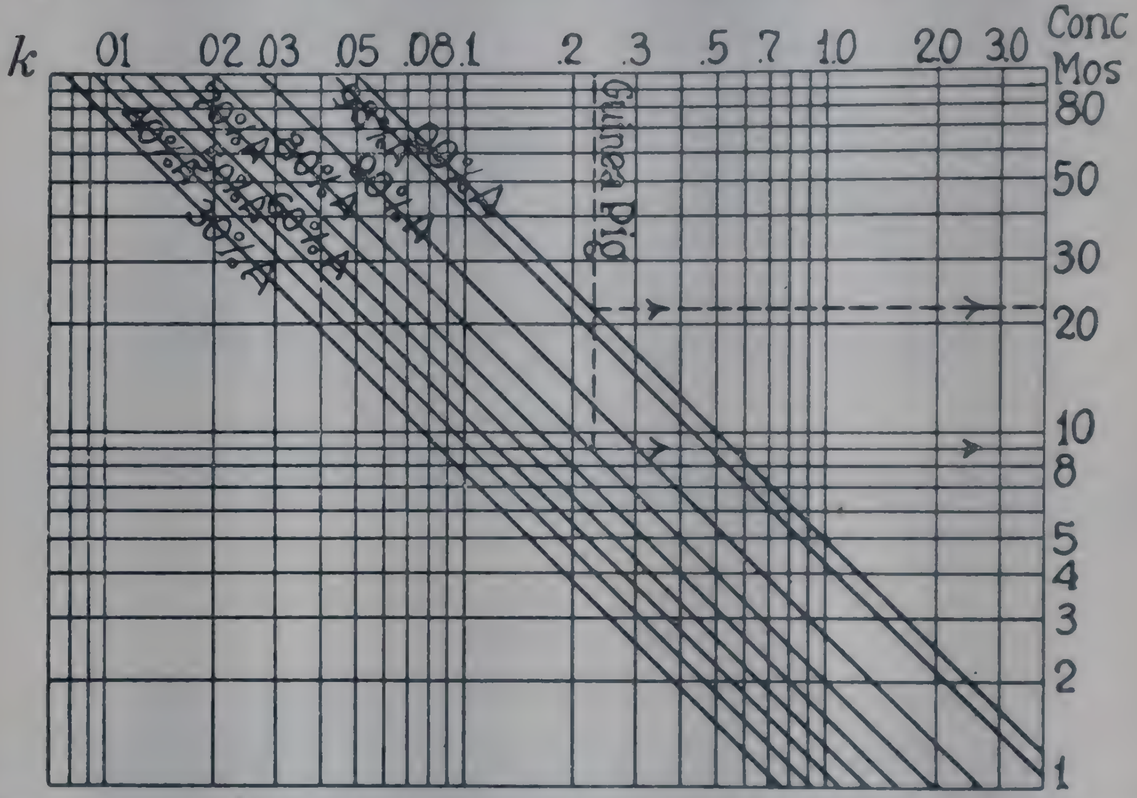

Fig. 19.10. This chart, showing the relation between the numerical value *k* and age at which a given fraction of the mature weight is reached, supplements Table 19.3. To illustrate the use of this chart, if the value of *k* is .23 (this is the value of *k* for the guinea pig), the chart shows that the animal reaches 99 per cent maturity (99 per cent A) at 22 months; 80 per cent A, at 9 months (from conception), and so on.

Some drugs affect the psychological-time scale. Thus at a certain stage in marihuana intoxication one's notion of time undergoes a change. The flow of time "appears infinitely slow, owing to the number and variety of impressions which rapidly enter the mind, and, since time is measured only by the memory of them, it seems infinitely long."[7] The distorted time scale in dreams offers similar illustration. The "relaxing" influence of alcohol may also be associated, in part, with a change in physiologic-time scale.

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[5] Hoagland, H., "The physiological control of judgement of duration," *J. Gen. Psychol.*, **9**, 267 (1933). Hoagland, H., and Perkins, C. R., "Some temperature characteristics in man," *J. Gen. Physiol.*, **18**, 399 (1934–5).

[6] Francois, Marcel, "Sur l'influence de la témperature interne sur notre appreciation du temps," *C. R. Soc. Biol.*, **98**, 152 (1928). Barcroft, J., "The Brain and Its Environment," Yale Press, 1938.

Changing environmental temperature changes the physiologic-time clock in cold-blooded animals in accordance with the van't Hoff-Arrhenius rule. The rates of feeding, growth, senescence, duration of life,[8] and energy metabolism in insects and other cold-blooded animals vary with temperature in accordance with this rule (Fig. 11.1 and Sect. 11.3).

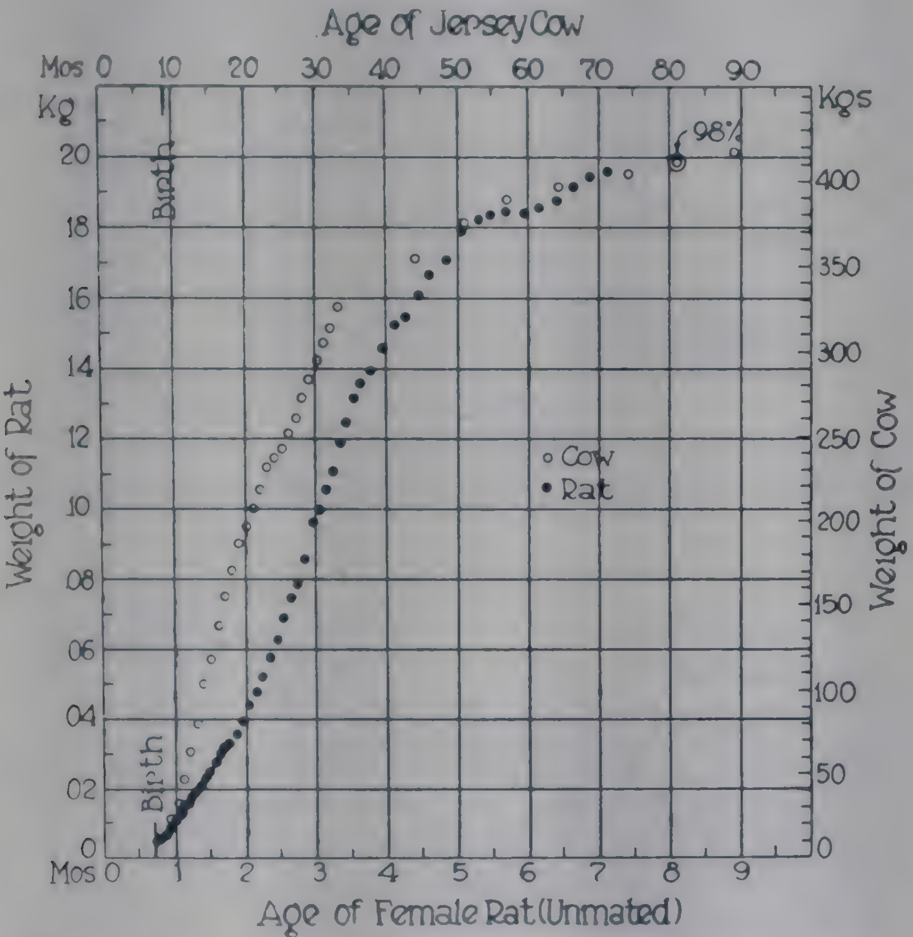

Fig. 19.11. Growth equivalence of cow and rat based on the assumption that the age when 98 per cent mature weight, A, is reached is equivalent in the two species (compare to Fig. 19.6).

Among the other possible controls of flow of physiologic time are thyroidectomy and thyroxine administration (Fig. 19.1), hypophysectomy, sickness, exercise, food supply (Figs. 19.16 to 19.20, and 16.30 to 16.38).

Different individuals and different organs of the same individual grow, mature, and age at different rates. Most biologic research (nutritional,

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[7] Adams, R., "Marihuana," *Science*, **92**, 115 (1940).

[8] Loeb, J., and Northrop, J. H., "Is there a temperature coefficient for the duration of life?", *Proc. Nat. Acad. Sci.*, **2**, 456 (1916), and **3**, 382 (1917); *J. Biol. Chem.*, **32**, 10 (1917), Loeb, J., *Sci. Monthly*, **9**, 578 (1919):

Temperature (°C).	10	15	20	25	30
Duration of life in *Drosophila*, days	178	124	54	39	21

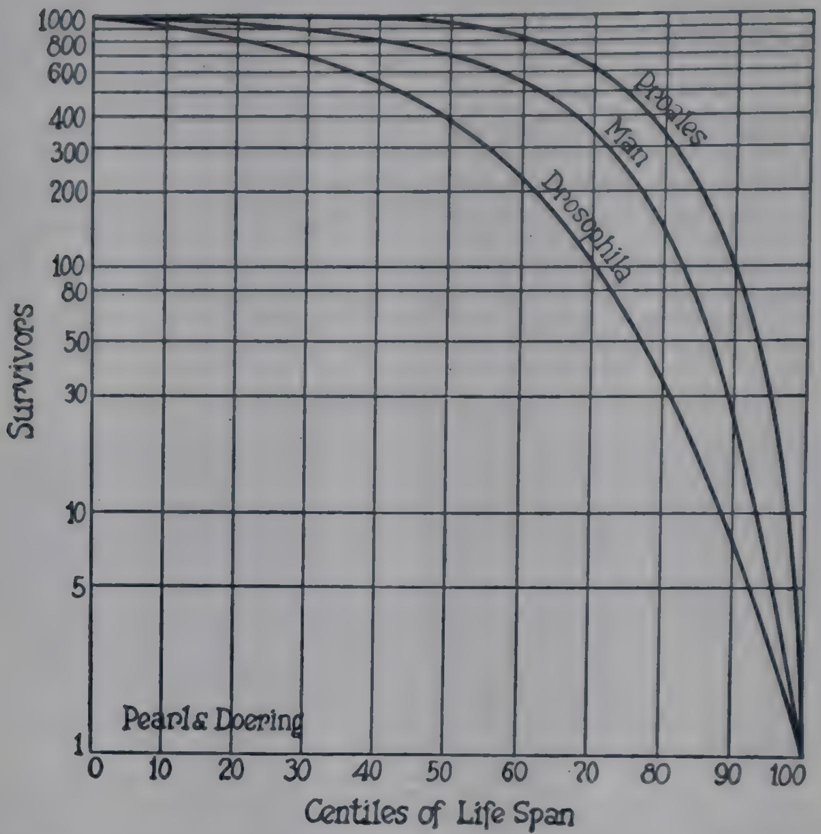
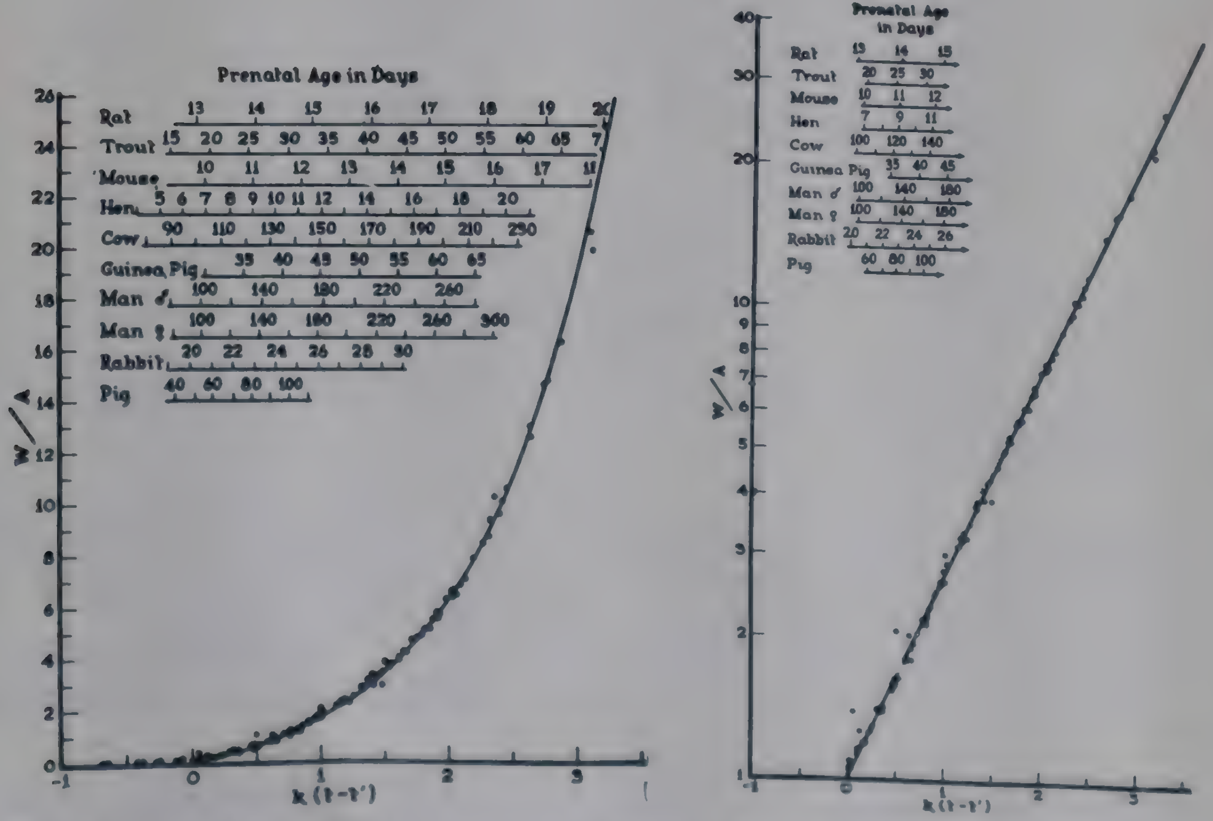


Fig. 19.12. Pearl and Doering's method of representing age equivalence.



Figs. 19.13a and b. Equivalence curves of prenatal growth in weight, plotted on arithmetic and logarithmic grids. Courtesy of A. P. Weinbach, and of *Growth*, 5, 230–1 (1941).

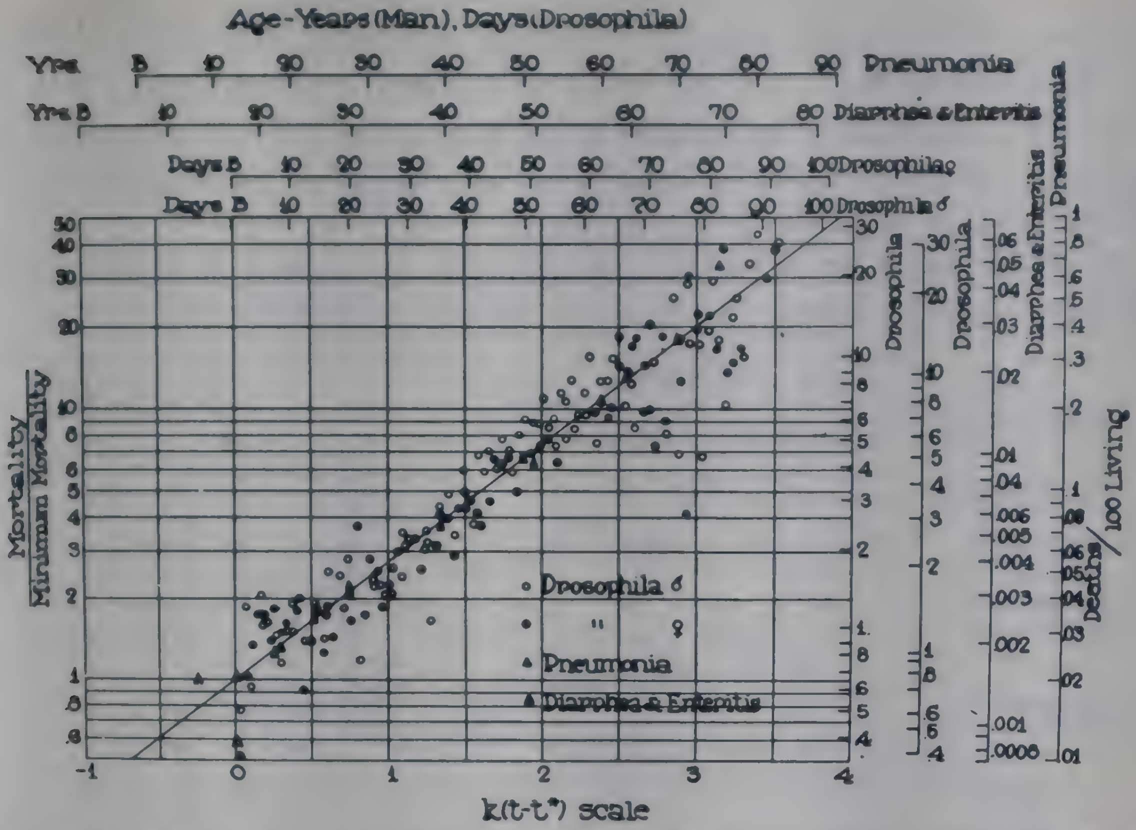


Fig. 19.14a. Equivalence of age in man and fruit fly (*Drosophila*) obtained by superimposing the age curves of relative specific mortality in the two species. The causes of death (pneumonia, diarrhea and enteritis) are indicated for man.

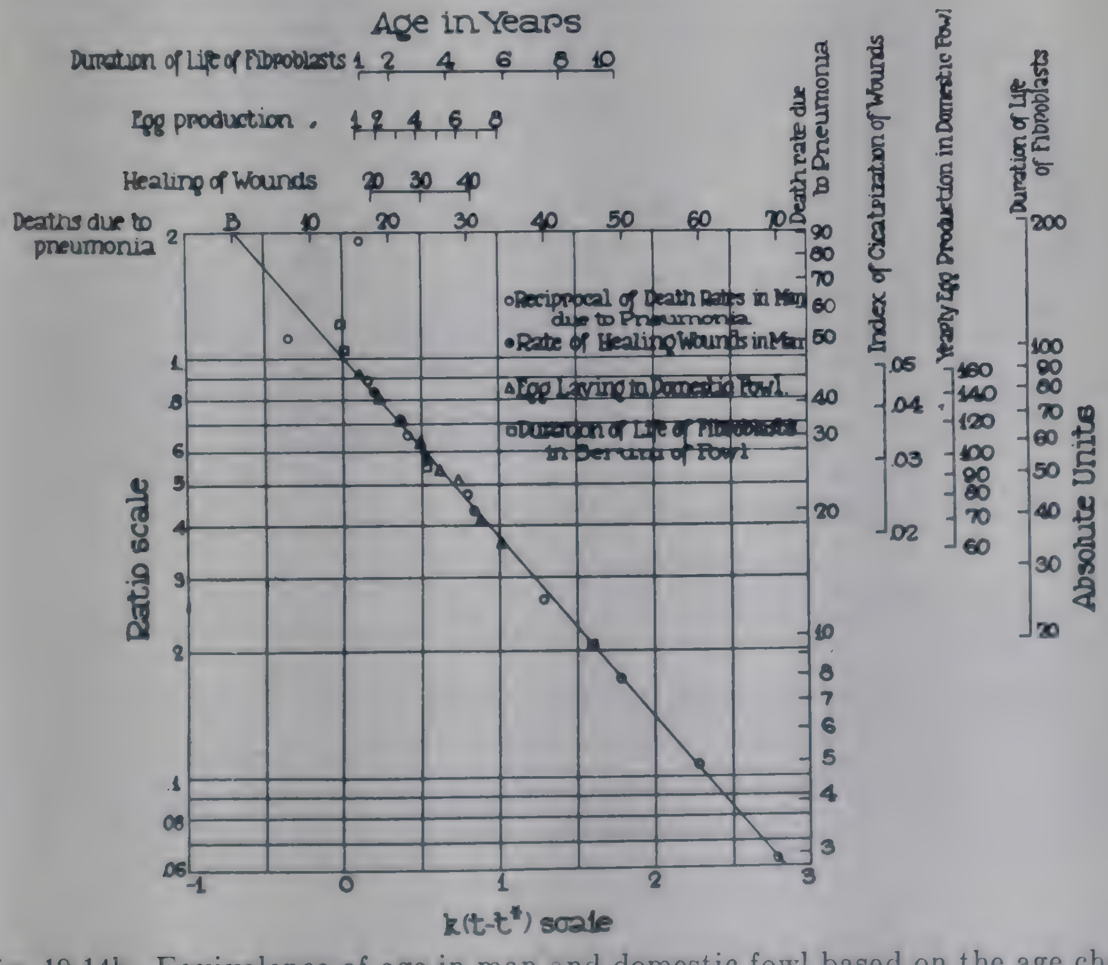


Fig. 19.14b. Equivalence of age in man and domestic fowl based on the age changes in specific mortality (from pneumonia) and healing of wounds in man, and egg laying and duration of fibroblasts *in vitro* in the fowl.

endocrinal, medical, agricultural) is indeed concerned, directly or indirectly, with the mechanisms of these rate differences, so engrossing personally, fascinating scientfically, and practical agriculturally. Our ability to control these rates of growth, senescence, and so on, must necessarily await our understanding of underlying mechanisms.

This discussion of relativity of physiologic time raises questions concerning methods for evaluating age equivalence, which we discuss next.

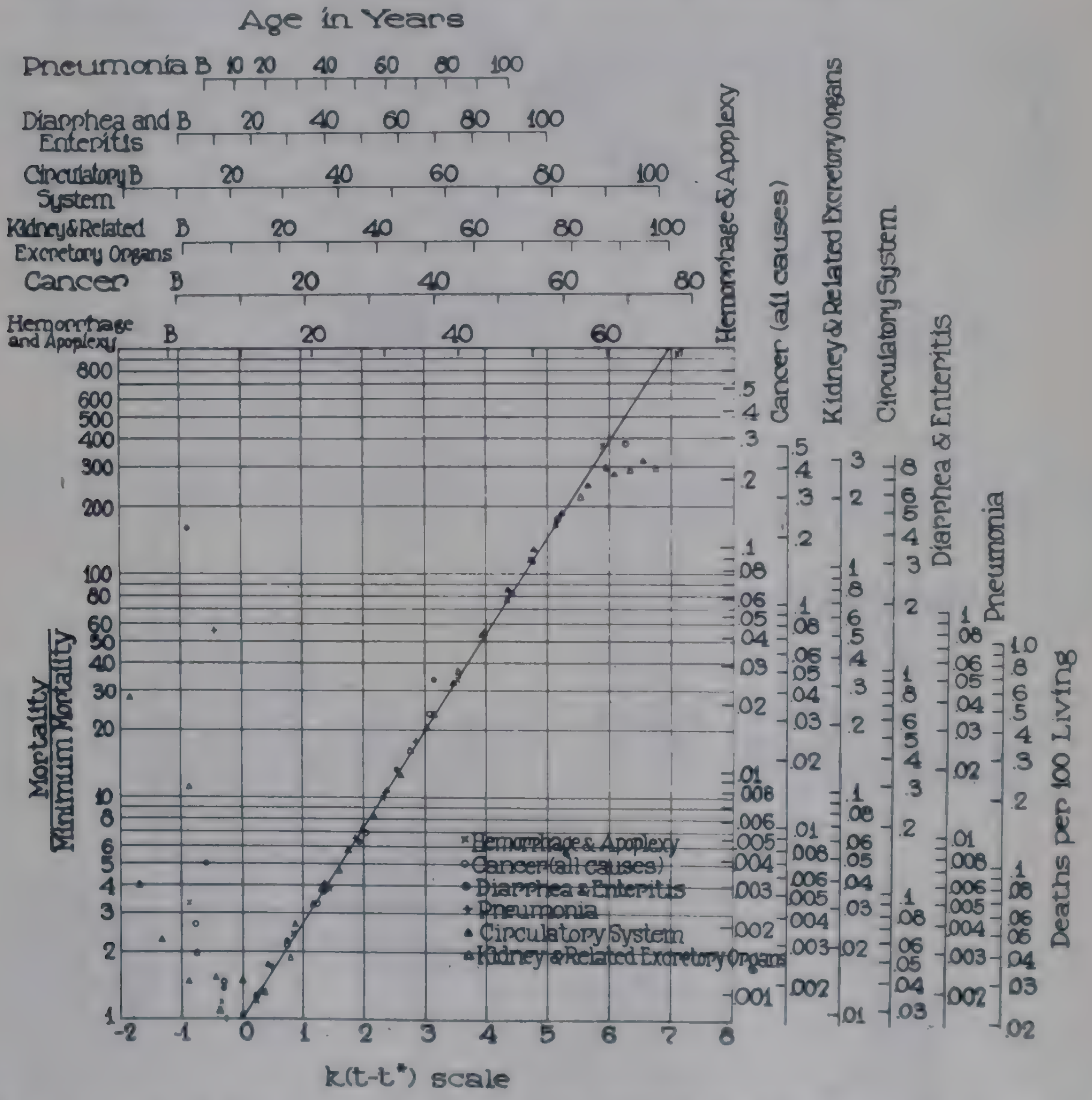


Fig. 19.15. Equivalence between human age curves of specific mortality due to different diseases.

19.2: Post-pubertal equivalence in weight growth.[9] As previously explained (Sect. 16.5), following the major (pubertal) inflection, the growth velocity, dW/dt, declines at a constant relative rate, k, with respect to growth yet to be made, $A - w$, as indicated by the differential equation

$$dW/dt = k(A - W) \tag{16.9}$$

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[9] Brody, S., "Relativity of physiologic time," *Growth*, **1**, 60 (1937). Brody, S., Sparrow, C. D., and Kibler, H. H., "Equivalence of age," *J. Gen. Physiol.*, **9**, 285 (1926). Brody, S., Univ. Mo. Agr. Exp. Sta. Res. Bull., 102, 1927.

or by the integral equation

$$W = A - Be^{-kt} \tag{16.12}$$

or by the equation

$$W/A = 1 - e^{-k(t - t^*)} \tag{16.14}$$

in which W is the size or weight of the organism (or population) at age t; t^* is the age at which the extrapolated post-pubertal curve cuts the age axis, A is mature weight; $(t-t^*)$ is, of course, age counted from t^*, and W/A is the fraction of mature weight attained at the age t (Ch. 16).

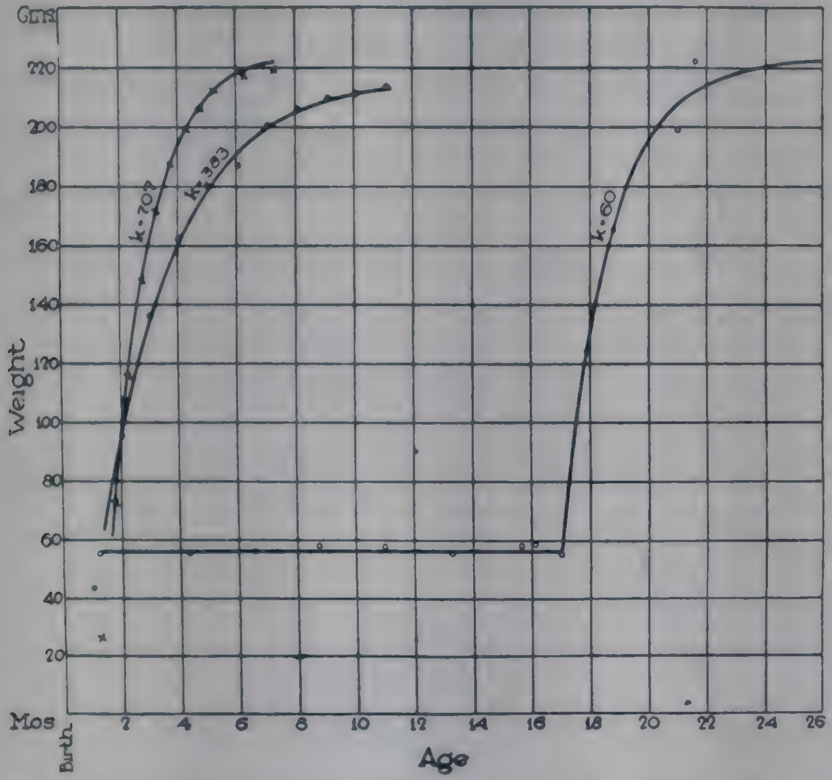

Fig. 19.16. The suppression and resumption of growth—that is of flow of growth time—in one rat by dietary manipulation, with a comparison to normally-fed rats. The charts were prepared from data furnished by Dr. T. B. Osborne in 1928. See also Osborne, T. B., and Mendel, L. B., The suppression of growth and the capacity to grow. *J. Biol. Chem.*, **18**, 95, (1914). The resumption of growth after long continued failure to grow. *Id.*, **23**, 439 (1915).

These equations furnish a precise method for computing equivalent time changes if the changes are exponential.

The speed of approach to the limiting or mature weight, A, is directly proportional to the numerical value of the relative growth rate, k, and the relative chronological durations of physiologically equivalent time intervals are, therefore, inversely proportional to the numerical values of the k's. Thus from Table 16.1, the numerical value of $100k$ of the Jersey cow is 5.4 and of the female white rat, 64.4; one month in the rat is, therefore, physiologically equivalent to $1 \times \frac{64.4}{5.4} = 11.9$ months in the cow; or one month in the cow is physiologically equivalent to $1 \times \frac{64.4}{5.4} = 0.08$ month in the rat.

This does not mean, however, that a 1-month rat is physiologically as old as an 11.9-months old cow, because the post-pubertal equivalence scales may differ from the pre-pubertal.

As a matter of fact, the former differ from the latter for the cow and rat (Fig. 19.2), but are the same for the cow and guinea pig (Fig. 19.3). The rat, but not the guinea pig, has a relatively longer pre-pubertal growth segment than the cow. Man has a pre-pubertal segment which is relatively still longer, so that if the age curves of man and other species are made to coincide post-pubertally they do not coincide pre-pubertally, as indicated by Figs 16.7, 19.4, 19.5, and 19.6.

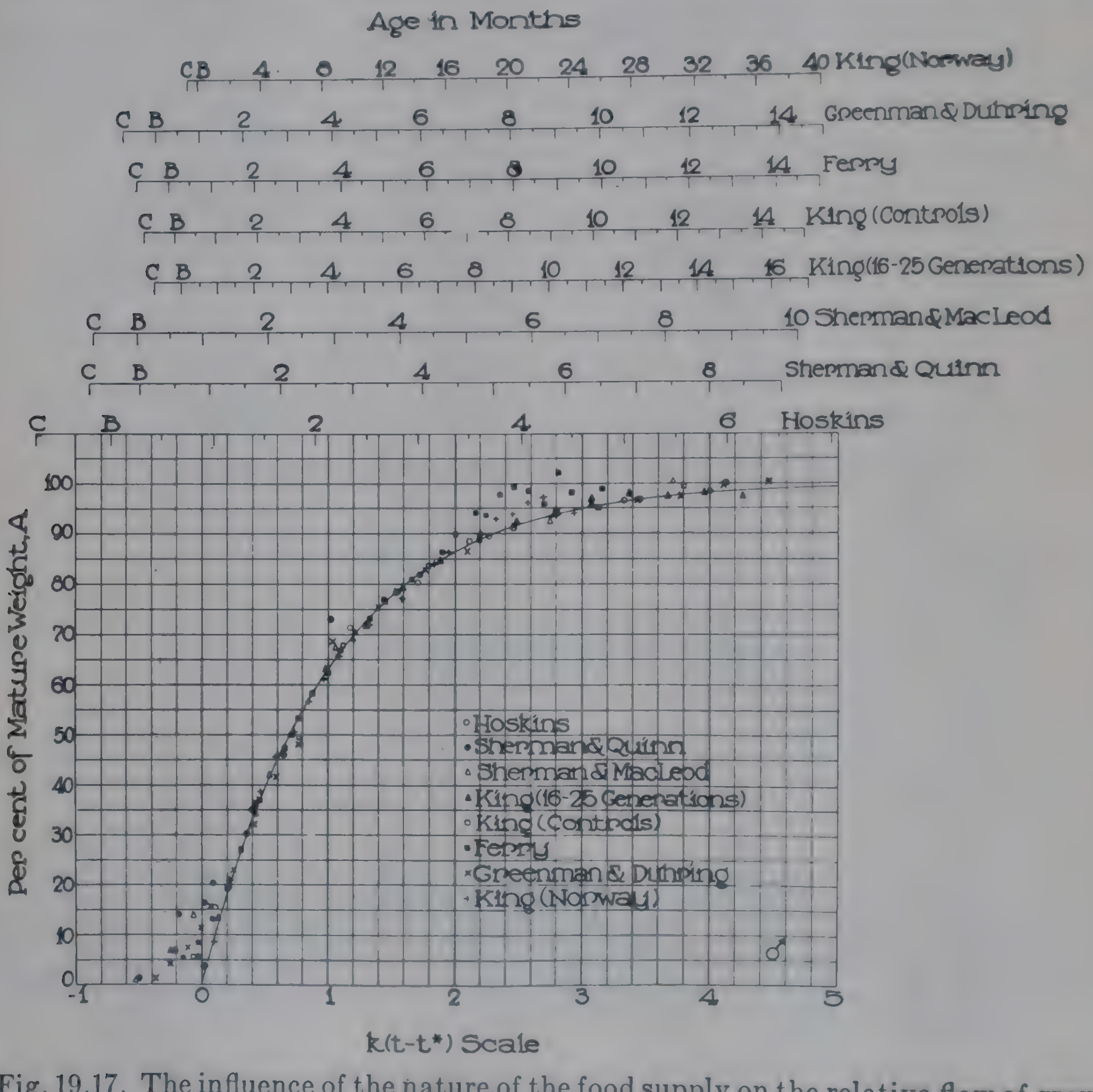

Fig. 19.17. The influence of the nature of the food supply on the relative flow of growth age in rats. While the mature weight was approached at the same rate in Hoskin's and in Osborne and Mendel's rats, the mature weight of Hoskin's rats (fed ductless glands) was 230 grams, and Osborne and Mendel's 430 grams. Sherman's rats weighed 330 grams at maturity. Dr. Osborne furnished the original data for the Osborne-Mendel curves. See the bibliograph in Univ. Missouri Res. Bull. 96, for the original papers for the other data.

This means that conception cannot be taken as a point of reference in preparing post-pubertal equivalence charts. Instead, we take for the point of reference the age, t^*, when the curve of equation (16.12) cuts the age

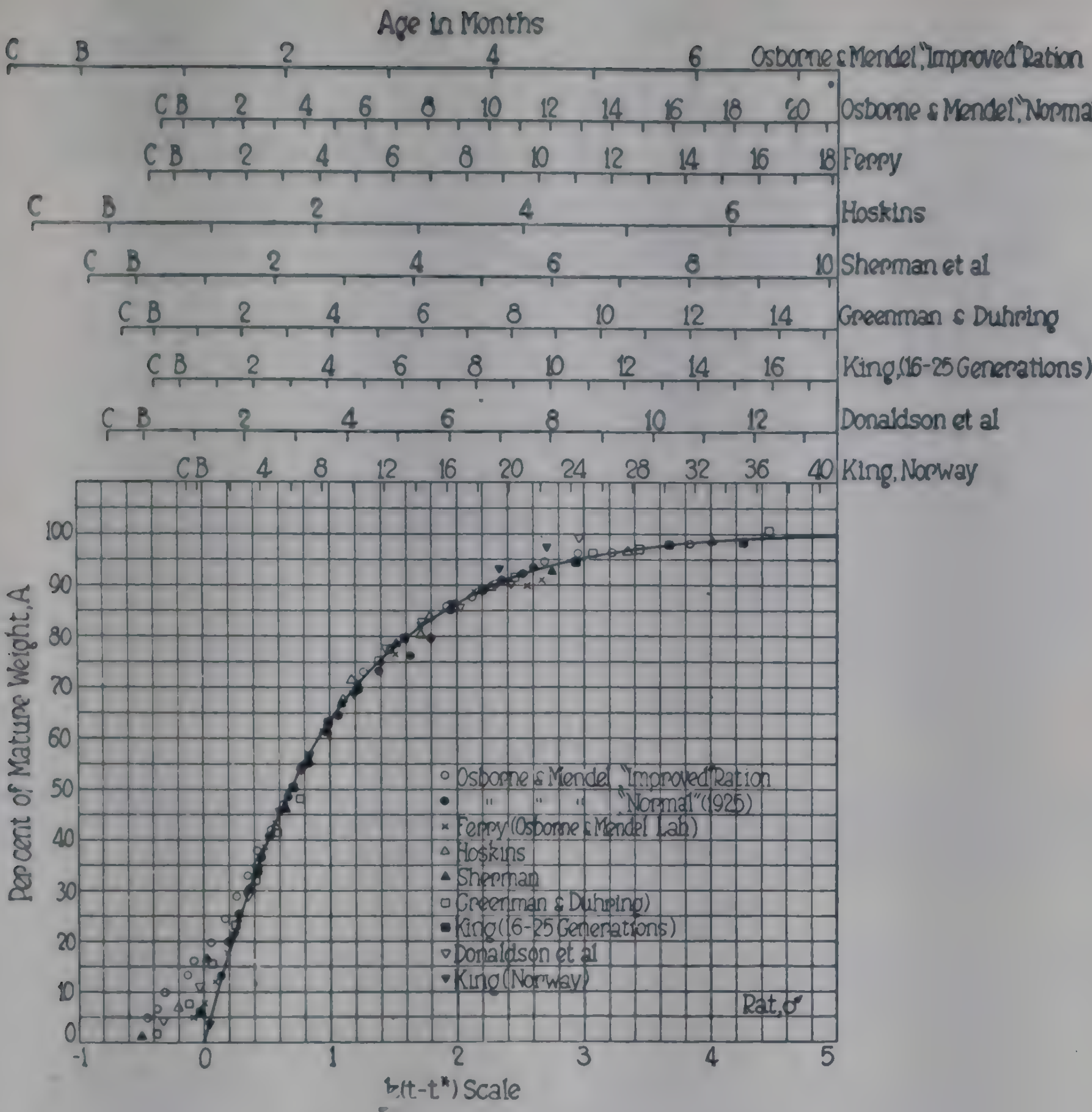

Fig. 19.18. See legend for Fig. 19.17.

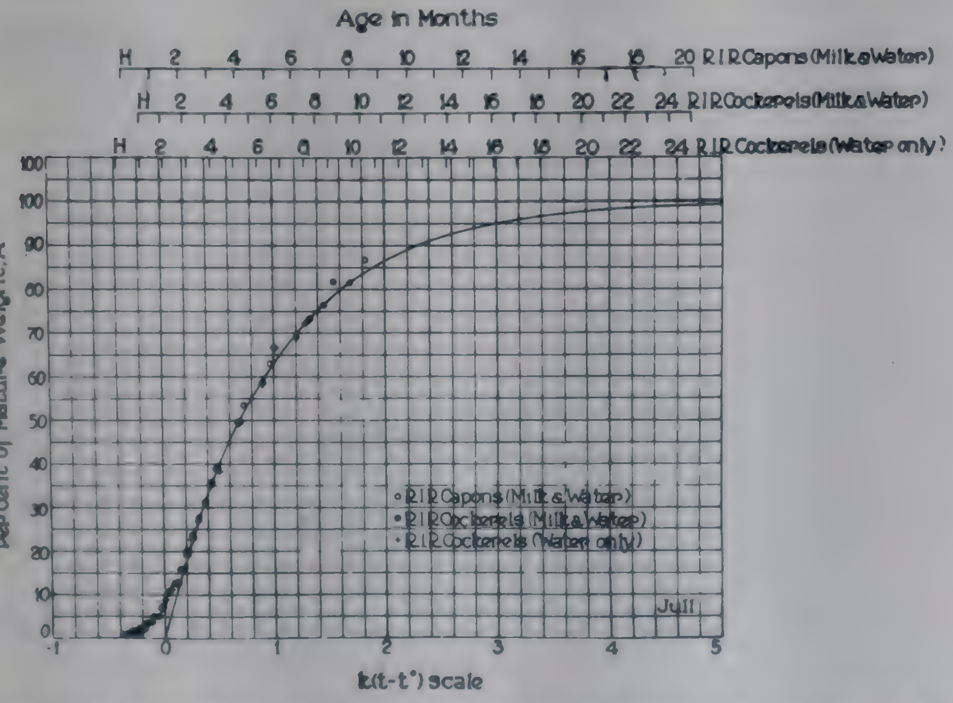

Fig. 19.19. The influence of milk in the diet and castration on the rate of approach to maturity in fowls. Data kindly furnished by Dr. M. A. Jull (see Univ. Missouri Agr. Exp. Sta. Res., Bull., 96, p. 114).

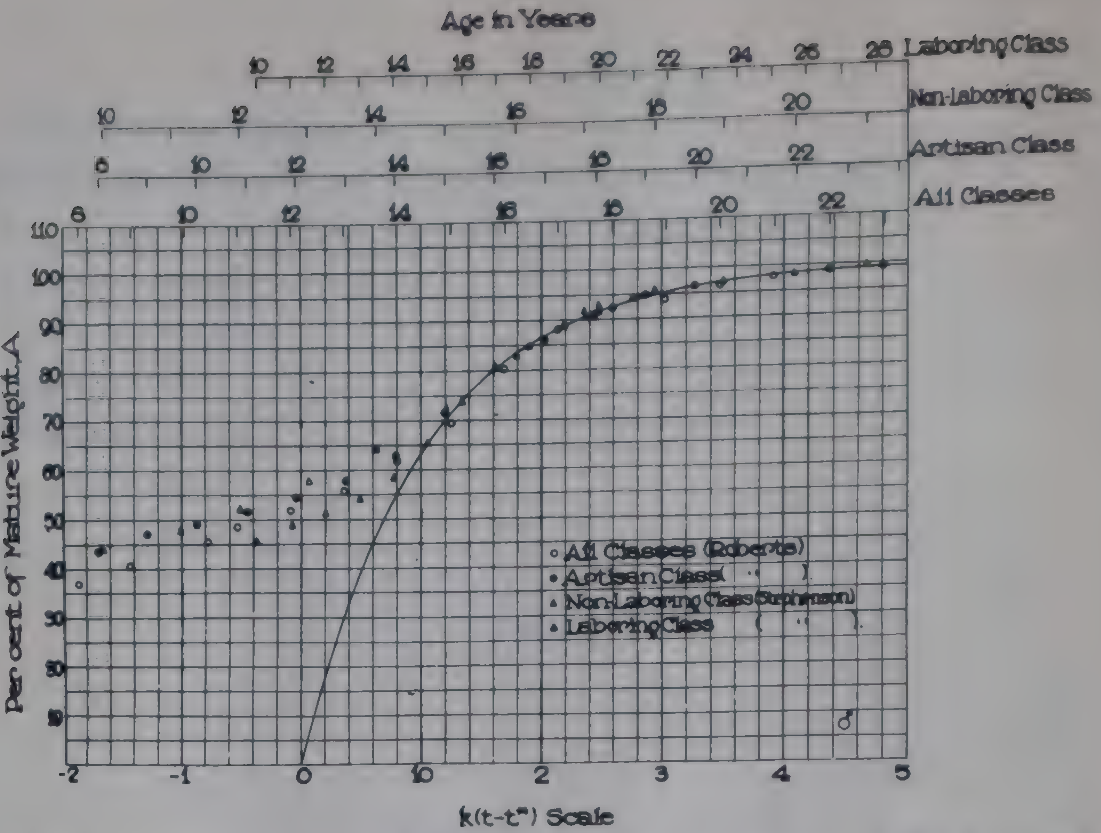

Fig. 19.20. Differences in rate of approach to mature weight of English children. Are these differences due to hereditary or environmental conditions? For the data see B. T. Baldwin, Univ. Iowa, *Studies in Child Welfare*, **1**, No. 1, (1931).

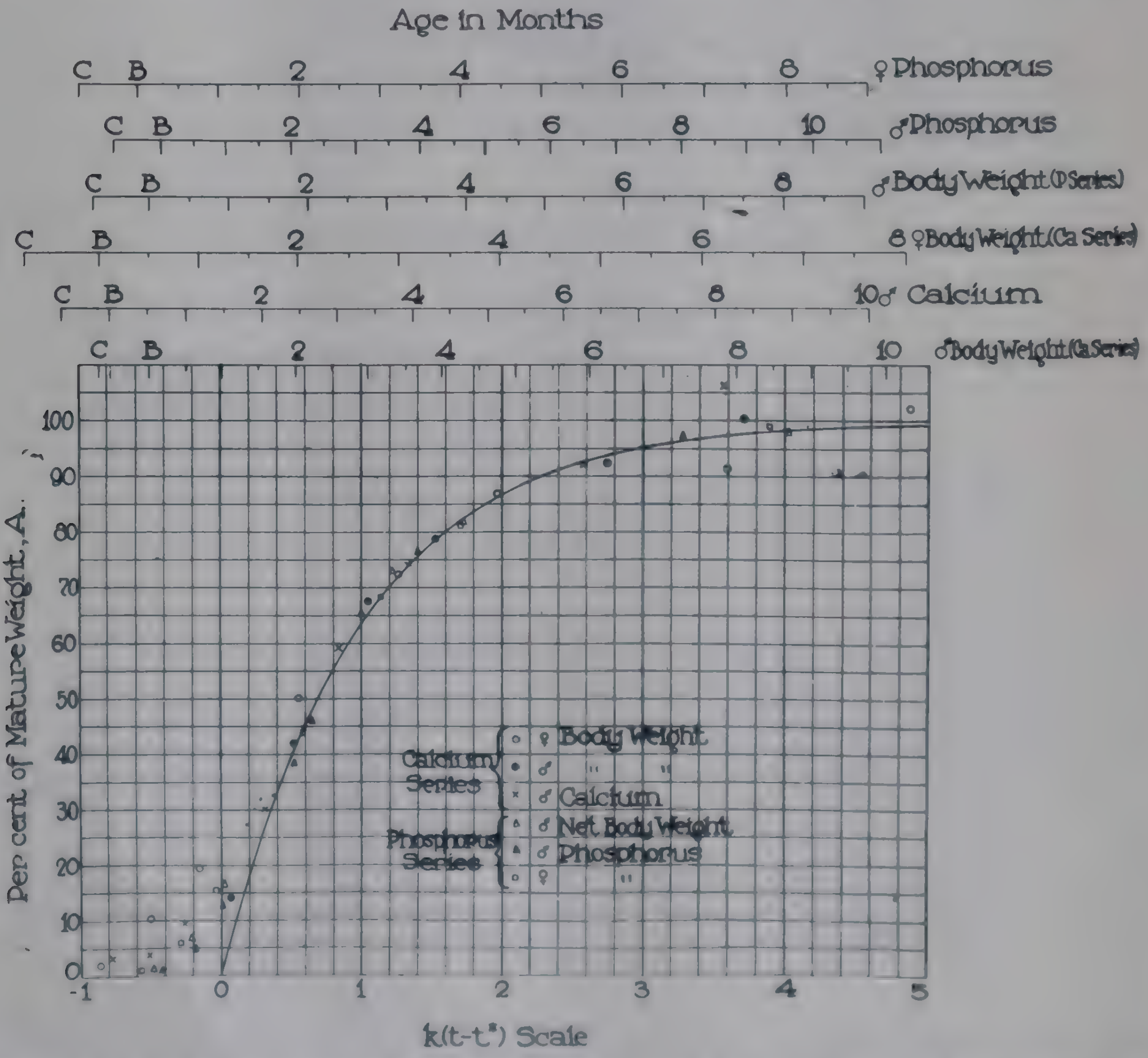

Fig. 19.21. Relative approach to maturity of total body weight, calcium, and phosphorus in the rat. For the data see Sherman, H. C., and Quinn, E. J., The phosphorus content of the body. *J. Biol. Chem.*, **67**, 667 (1926); Sherman and MacLeod, F. L., "The calcium content of the body." *Id.*, **64**, 424 (1925). For more recent data see Caroline Sherman Lanford, H. L. Campbell, and H. C. Sherman, *J. Biol. Chem.*, **137**, 627 (1941).

axis (explained and illustrated in Sect. 16.5; see especially Fig. 16.27, also Figs. 16.25 and 16.26). It is only after the age t^* that 1 month in the rat is

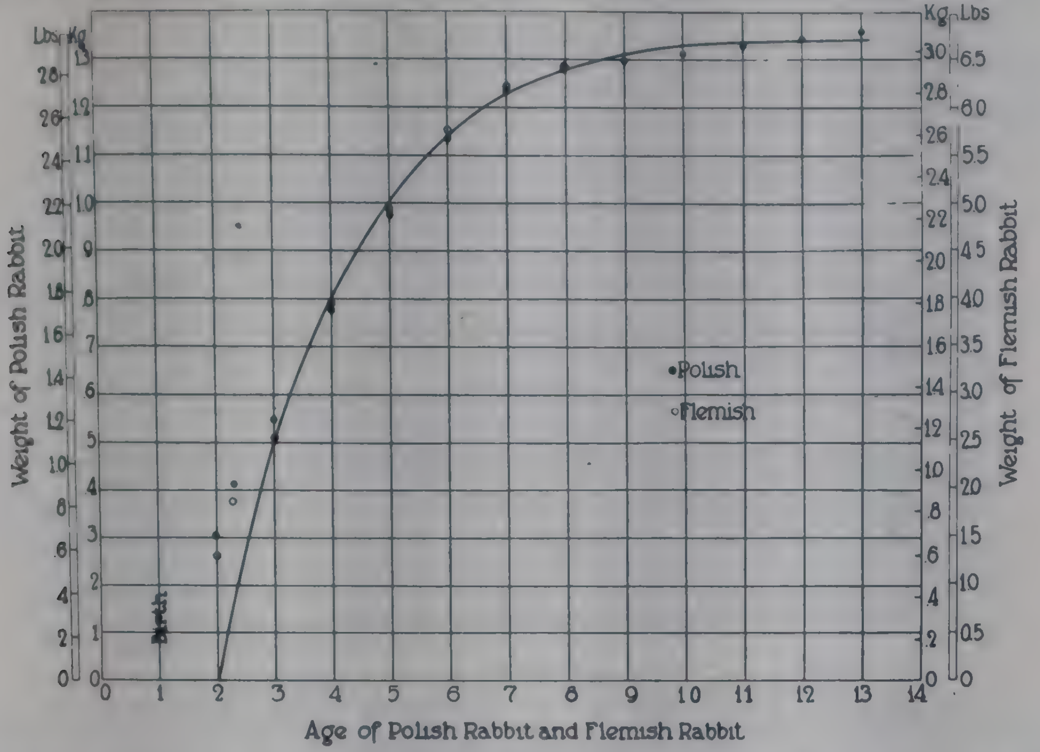

Fig. 19.22. Polish and Flemish rabbits approach mature weight at the same rate despite the great difference in mature weight of the two breeds of rabbits. From data by W. E. Castle.

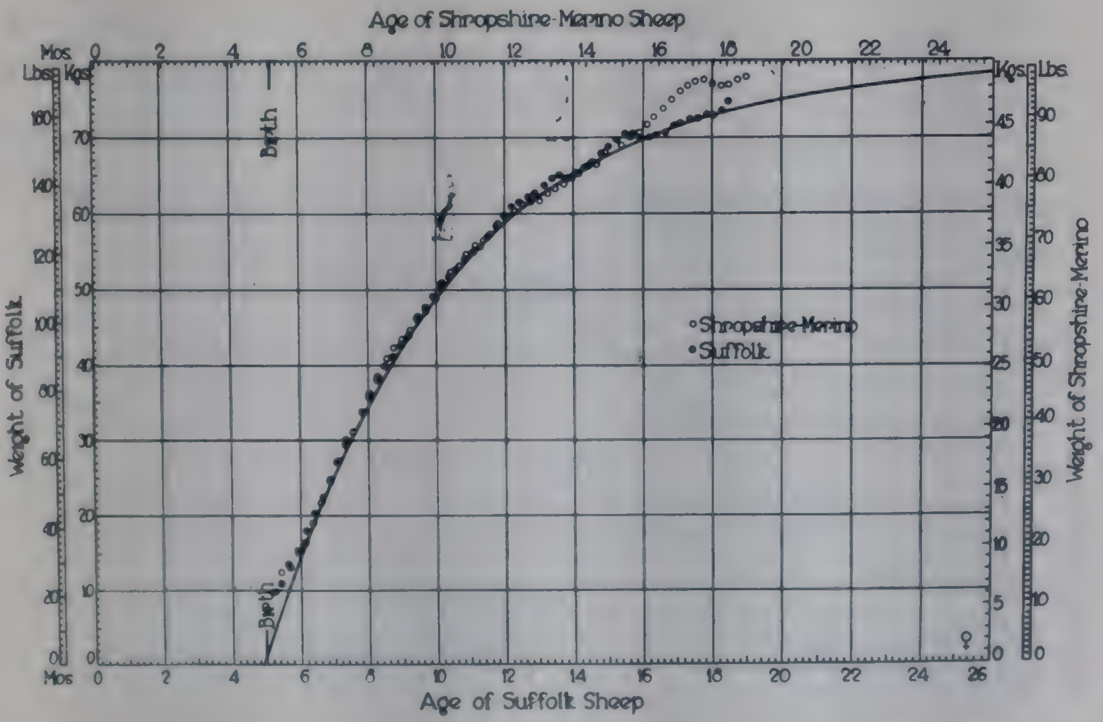

Fig. 19.23. Suffolk and Shropshire-Merino sheep approach maturity at the same rate despite differences in mature weight.

equivalent to 11.9 months in the cow. (The numerical value of t^* may be read from the graph of the equation fitted to the data as shown in Figs. 16.27, 16.25, 16.28; t^* is the age when $A - W = A$, just as B is the value of A

$- W$ when $t = 0$; or t^* may be computed algebraically as given by equations (13) to (15) in Chapter 16.)

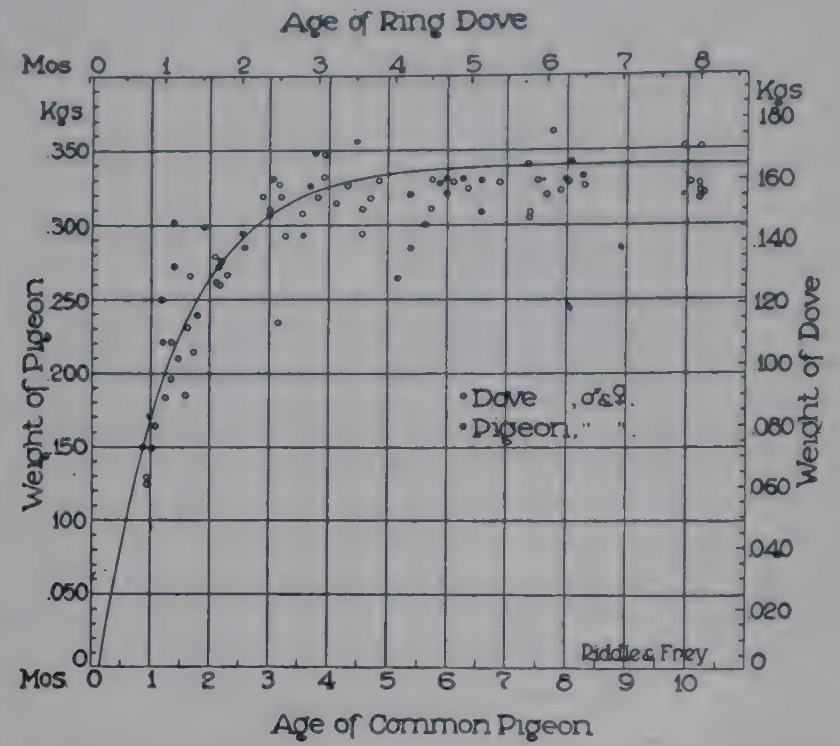

Fig. 19.24. Ring dove and common pigeon reach mature weight in nearly the same time despite differences in mature weight.

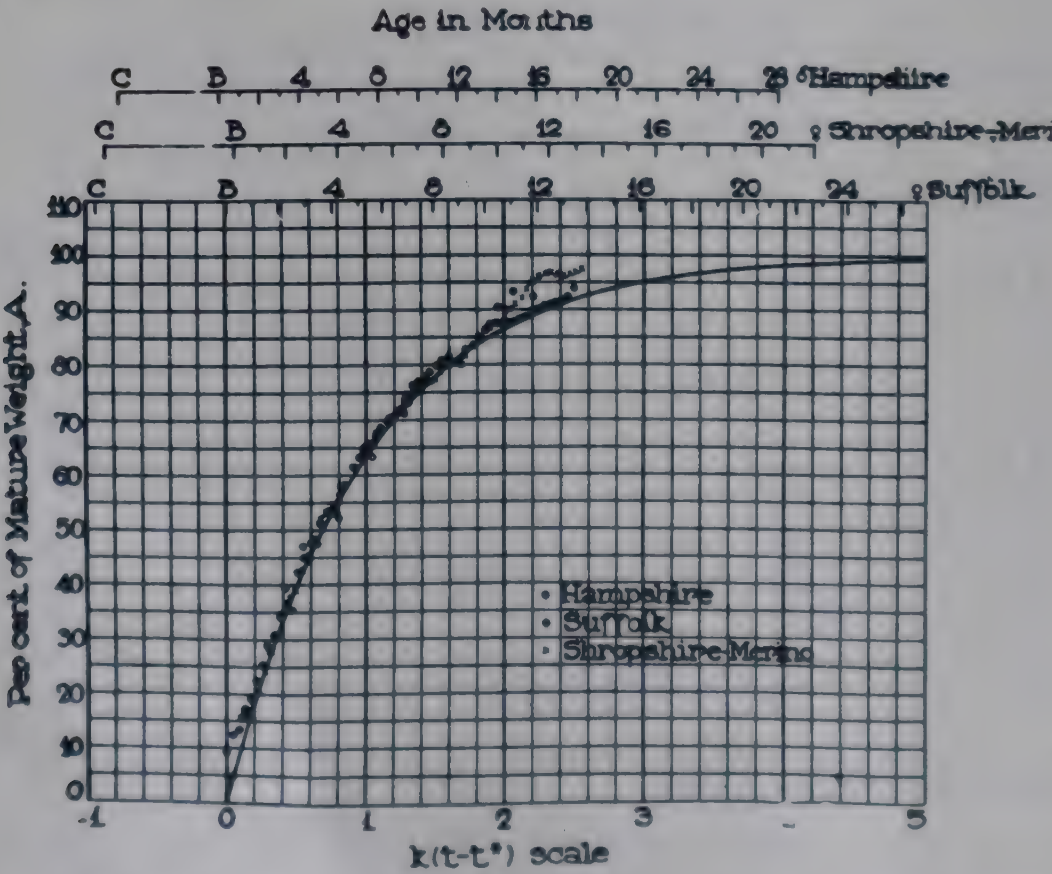

Fig. 19.25. These Hampshire sheep require a longer time to reach mature weight than the other two breeds.

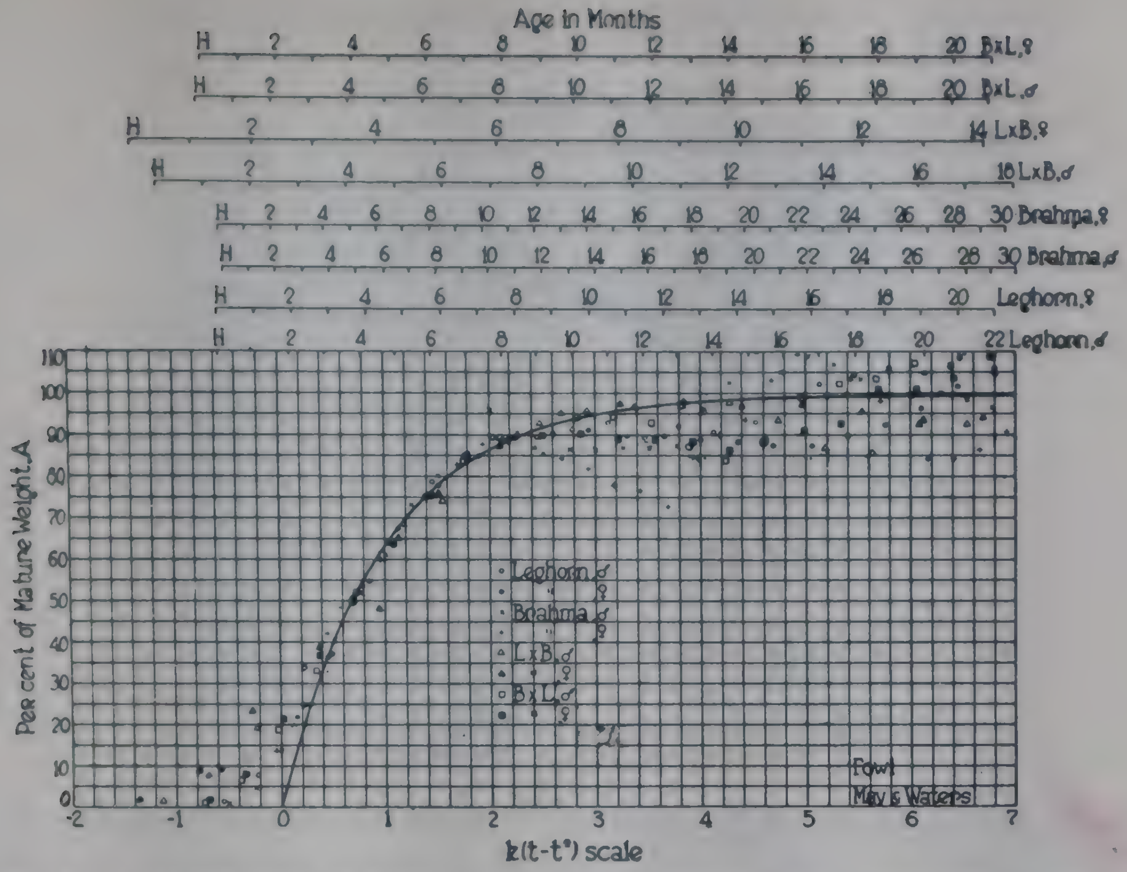

Fig. 19.26. Brahma fowls are much larger than Leghorn fowls, as shown in Fig. 16.49, and, unlike the Flemish and Polish rabbits (Fig. 19.22), Brahmas take much more time than Leghorns to attain mature weight. It is not, therefore, possible to generalize the relation between mature weight and time required to attain it.

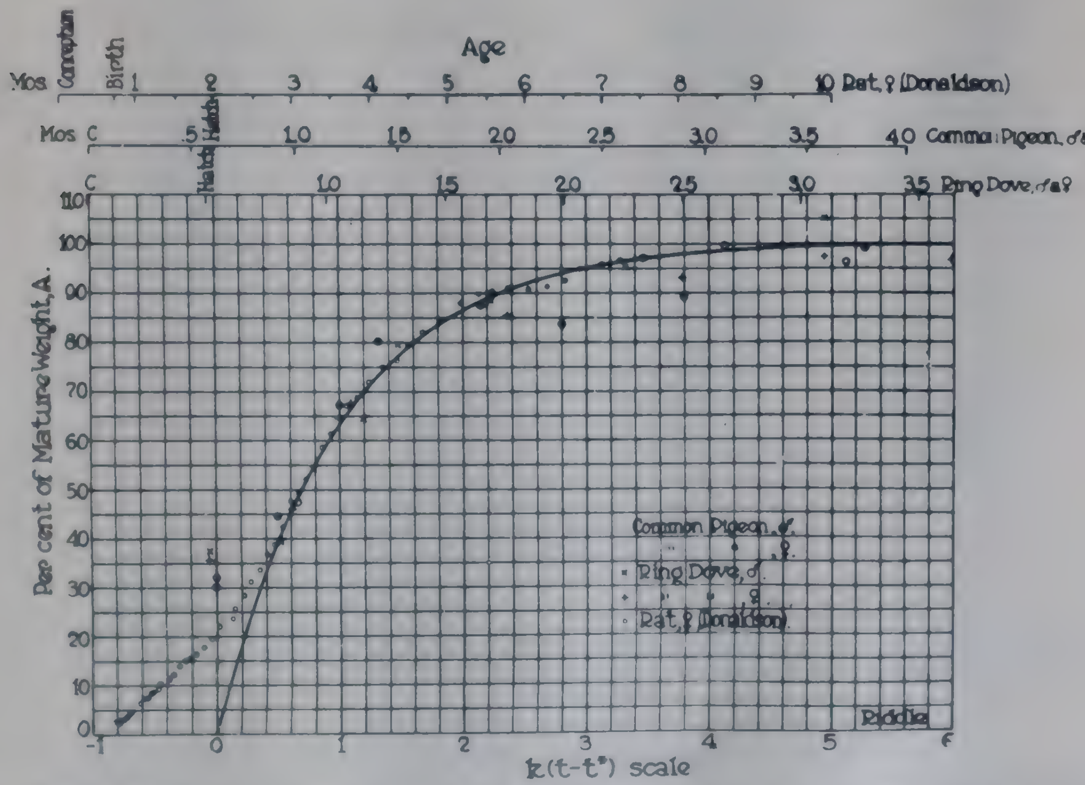

Fig. 19.27 Substantiates the legend to Fig. 19.26 that body weight and time required to attain it are not closely related. As shown in Fig. 16.48, rat, dove, and pigeon are roughly in the same weight class. Yet pigeon and dove reach mature weight much earlier than rat partly because of the longer infantile-juvenile period in the rat and partly because the rate, k, of approach to mature weight, A, is more rapid in the pigeon and dove than in the rat. (See Table 16.1 for the numerical values of k and A.)

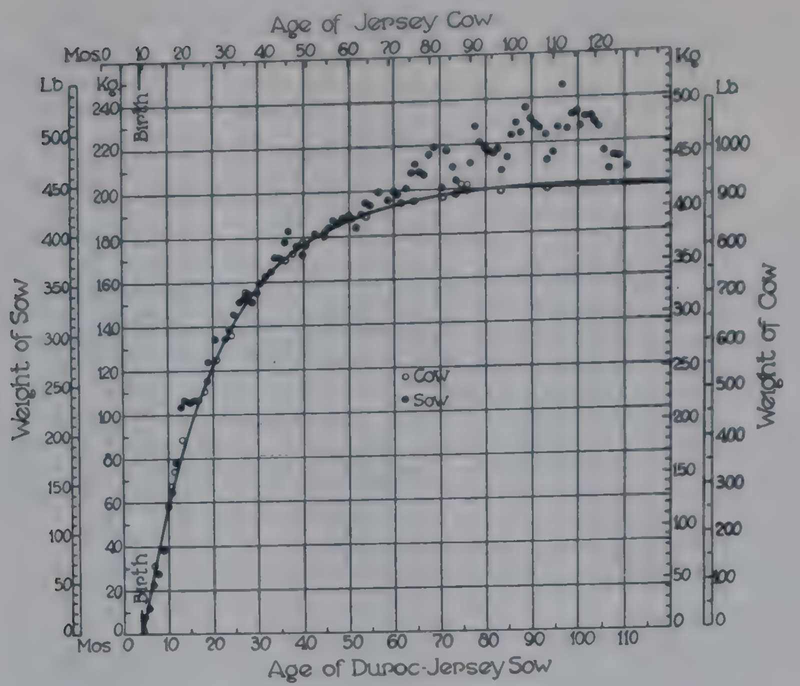

Fig. 19.28. Equivalence of age based on the proportionality of the mature weights, A, and rate of growth k, with t^* as null point.

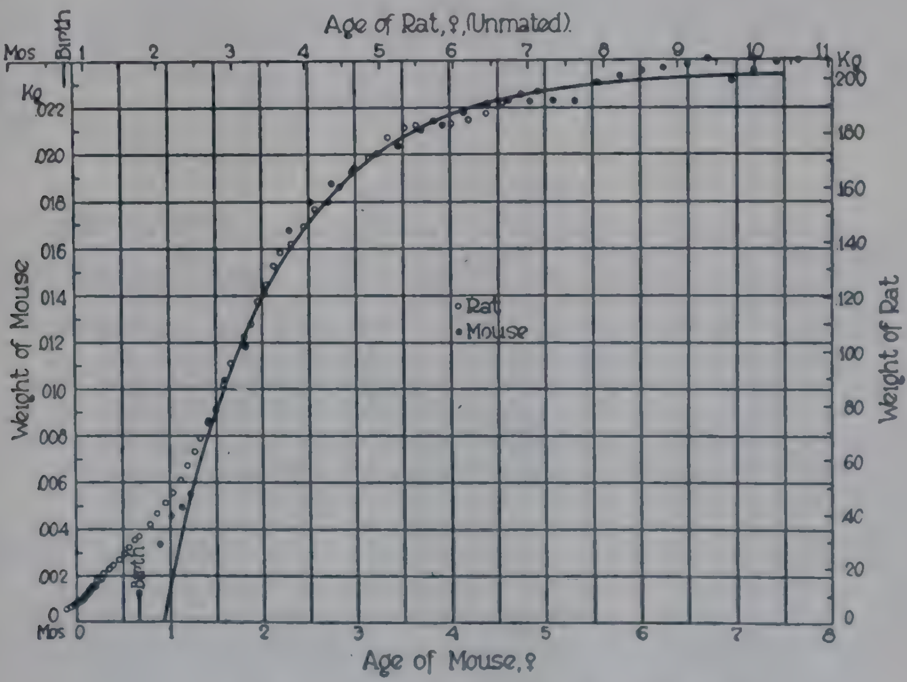

Fig. 19.29. See legend for Fig. 19.28.

By way of illustration, let us prepare an equivalence chart for the rat and cow previously discussed, having the following constants:

	A (mature weight) (kg)	k	t^* (mos.)
Jersey cow . . .	420.0	0.054	8.9
White rat	0.203	0.644	2.03

$$\text{Age factor} = \frac{0.644}{0.054} = 11.9$$

For the first pair of age-equivalence, t^* is taken; for the second pair one may take, for example, 8 months from conception in the rat, which is 8.0 − 2.03 = 5.97 months from t^*. Now, 5.97 months in the rat is equivalent to 5.97 × 11.9 = 71.1 months from t^*, or 71.1 + 8.9 months from conception, in the cow. 8 months in the rat and 80 months

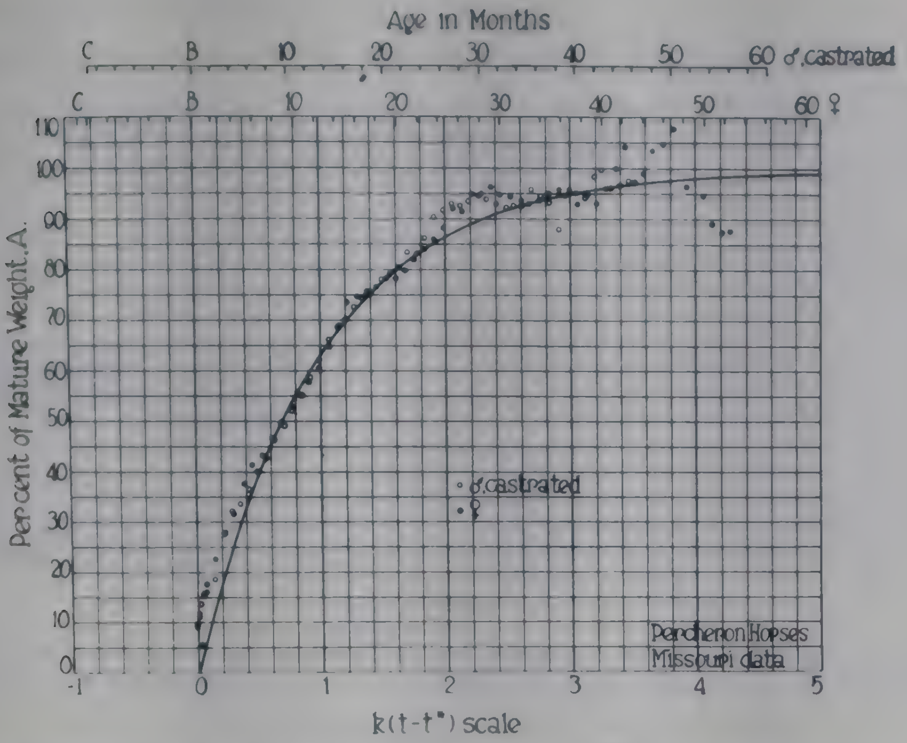

Fig. 19.30. Equivalence of age based on plotting $\frac{W}{A}$ against the equivalent-time scale $k(t - t^*)$.

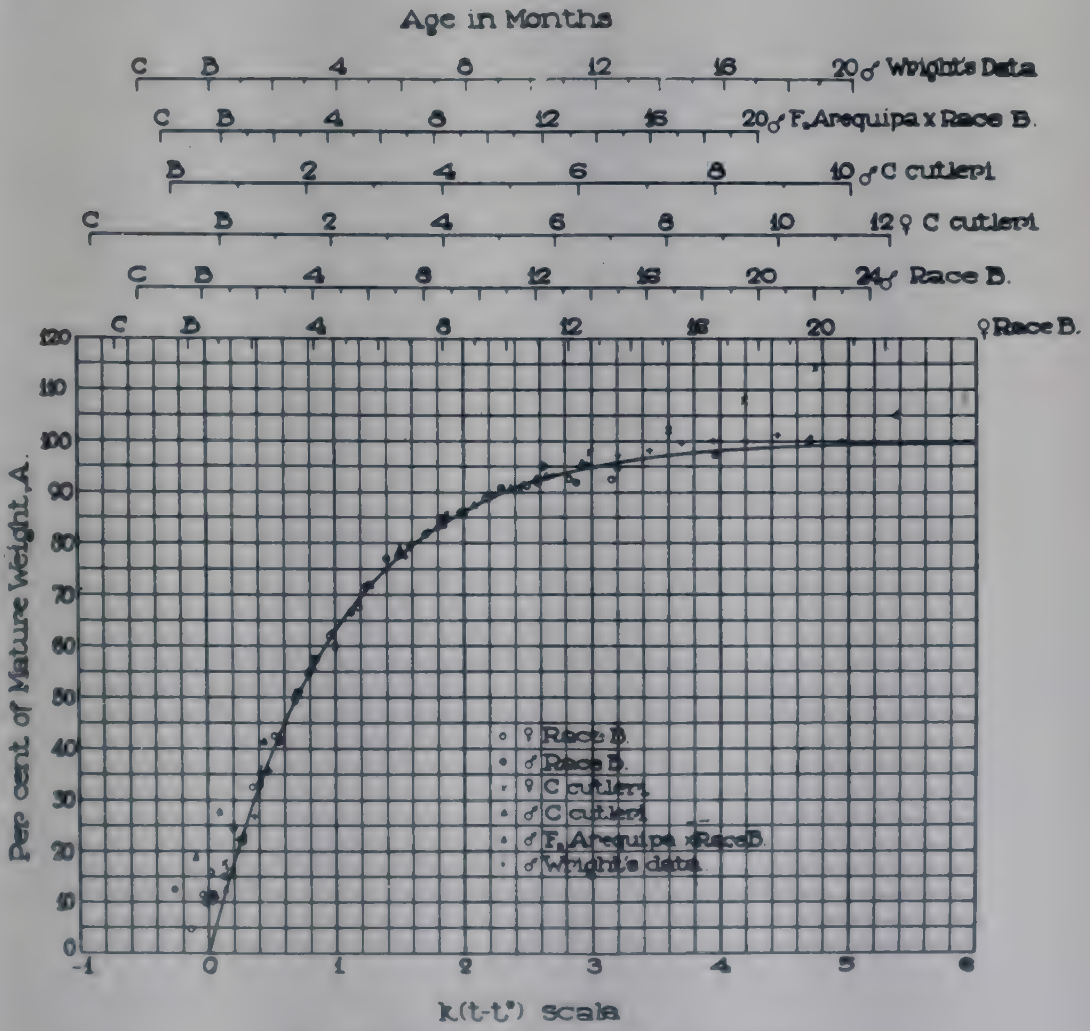

Fig. 19.31. See legend for Fig. 19.30.

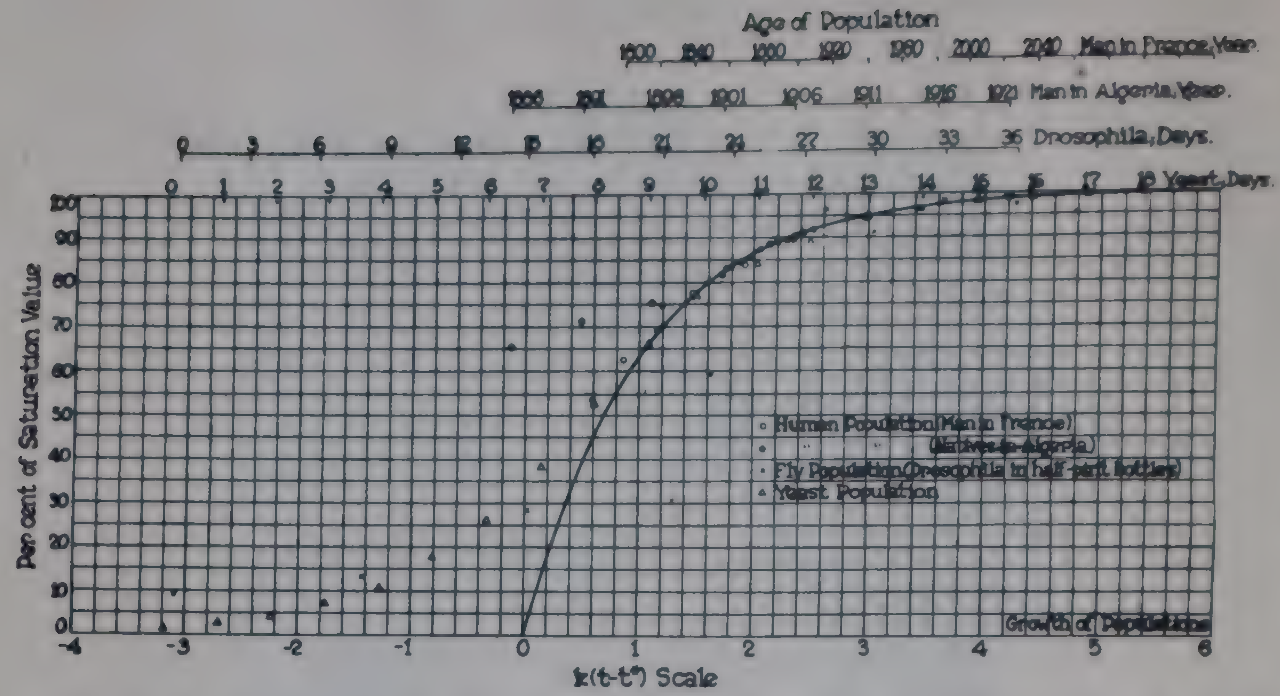

Fig. 19.32. Equivalence of increase in population of man, *Drosophila*, and yeast plotted against the equivalent-time scale $k(t - t^*)$. Compare to Fig. 16.5.

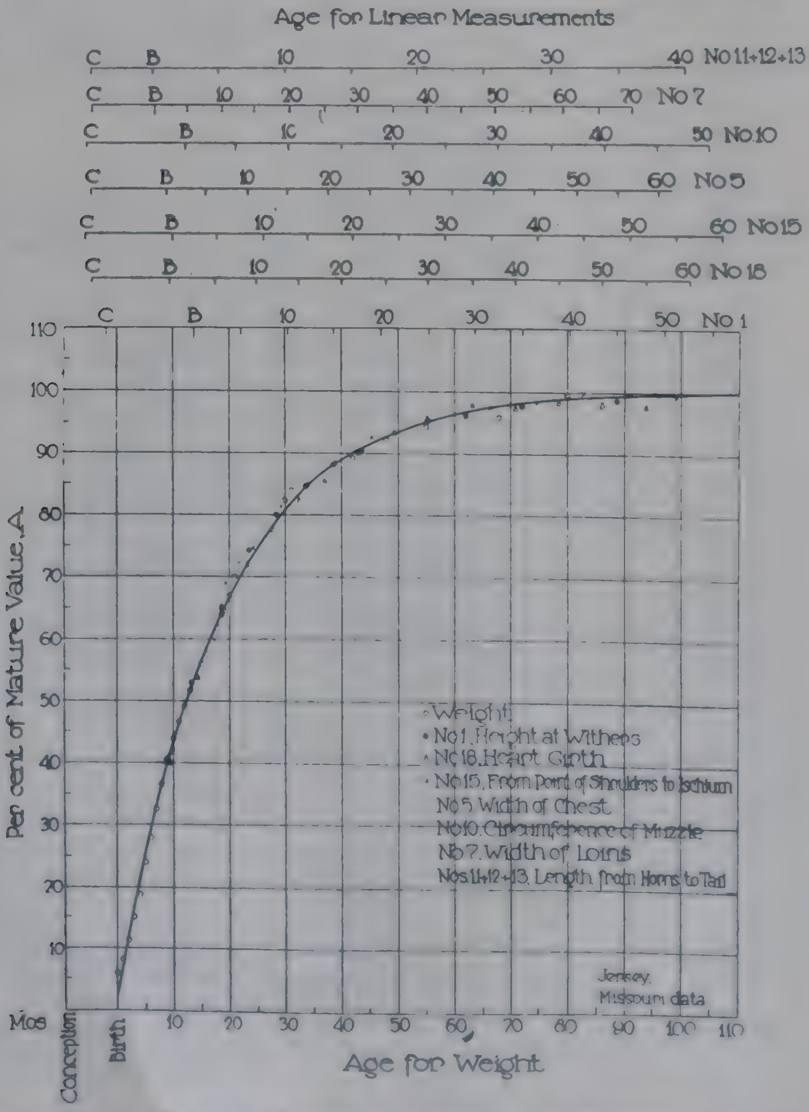

Fig. 19.33. Equivalence of age with respect to growth in weight and growth in linearly-measured dimensions in Jersey cattle. No. 1 represents height at withers; No. 18, chest girth; No. 15 distance from a point on shoulder to ischium; No. 5 width of chest; No. 10 circumference of muzzle; No. 7 width of loin; No. 11 + 12 + 13 distance from horns to tail. See Fig. 17.11 for a graphic representation of these measurements.

in the cow, both counted from conception, thus constitute the second pair of growth-in-weight equivalent points. For weight equivalence, one reference point for both species is zero; the other, is the value of A, 420 kg for the cow and 0.203 kg for the rat. Having the reference points on the chart, the intermediate points are graduated uniformly and extrapolated if desired. The proof of the correctness of the above method is demonstrated by the good agreement between curves of widely different species in Figs. 19.2 to 19.5, and 19.7.

The method may be standardized for large-scale chart production by the use of equation (16.14). It states that for a given value of $k(t - t^*)$, there is one, and only one, value of W/A. If, therefore, values of W/A of different organisms are plotted against their corresponding $k(t - t^*)$ values, the resulting curves will necessarily coincide. After the data are plotted on the $k(t - t^*)$ grid, the absolute age scales are laid off, and the chart is completed. Equivalent ages for a given value of W/A may be read directly from the chart.

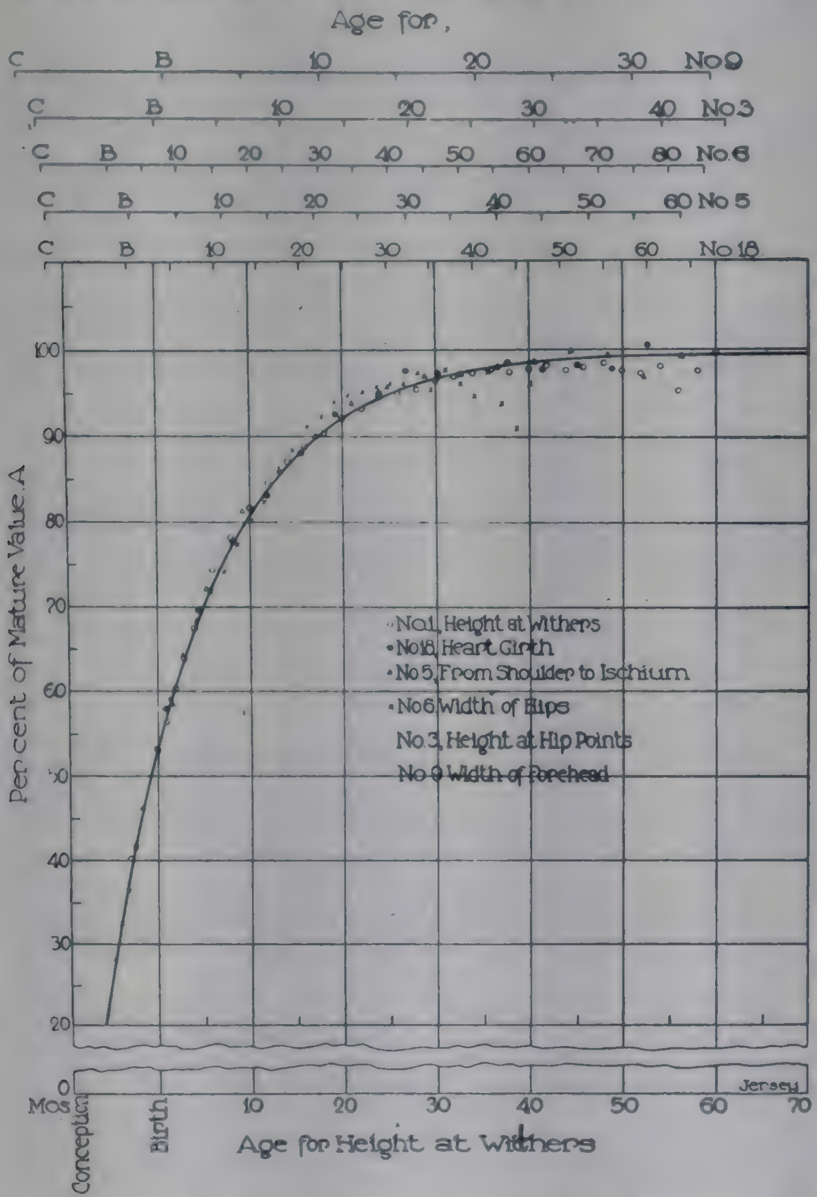

Fig. 19.34. Equivalence of age with respect to height at withers. No. 3 represents height at hip points; 6 width of hips; 9, width of forehead. For the other symbols see legends to the preceding chart.

If the curves for two organisms are on different charts, the equivalence may be estimated with reference to the corresponding values of $k(t - t^*)$. Thus, assume that it is desired to estimate the age of the mouse corresponding to 92 months in the cow; from Fig. 19.8, 92 months in the cow corresponds to 5 on the $k(t - t^*)$ scale of the cow, and from Fig. 19.9, the value of 5 on the $k(t - t^*)$ scale in the mouse corresponds to 6.4 months. Hence 6.4 months in the mouse is equivalent to 92 months in the cow.

To facilitate plotting the curve of equation (16.14), Table 19.1 is presented in which W/A values are given for corresponding $k(t - t^*)$ values. In the preparation of these charts, coordinate paper was used having 20 squares between 0 and 100. The values in the column headed by 20 W/A are given for plotting on such paper.

Table 19.1 may also be employed for estimating the approximate equivalence of age for two organisms by reading the values of $k(t - t^*)$ corresponding to given values of W/A (right of the heavy line).

Instead of reading the equivalent growth ages of two or more animals from a chart, one may compute the ages, t, at which desired values of W/A are reached in animals under comparison as described below.

The growth equation

$$W = A - Be^{-kt}$$

TABLE 19.1. Table of numerical values of W/A corresponding to different values of $k(t - t^*)$ in the equation $W/A = 1 - e^{-k(t-t^*)}$

$k(t - t^*)$	$e^{-k(t - t^*)}$	$\frac{W}{A}$	$\frac{20W}{A}$	$\frac{W}{A}$	$e^{-k(t - t^*)}$	$k(t - t^*)$
0	1.0000	.0000	0.000	.00	1.00	.000
.1	.9048	.0952	1.904	.05	.95	.051
.2	.8187	.1813	3.626	.10	.90	.105
.3	.7408	.2592	5.184	.15	.85	.162
.4	.6703	.3297	6.594	.20	.80	.223
.5	.6065	.3935	7.870	.25	.75	.288
.6	.5488	.4512	9.024	.30	.70	.357
.7	.4966	.5034	10.068	.35	.65	.431
.8	.4493	.5507	11.014	.40	.60	.511
.9	.4066	.5943	11.868	.45	.55	.598
1.0	.3679	.6321	12.642	.50	.50	.693
1.2	.3012	.6988	13.976	.55	.45	.799
1.4	.2466	.7534	15.068	.60	.40	.917
1.6	.2019	.7981	15.962	.65	.35	1.050
1.8	.1653	.8347	16.694	.70	.30	1.204
2.0	.1353	.8647	17.294	.75	.25	1.386
2.5	.0821	.9197	18.358	.80	.20	1.609
3.0	.0498	.9502	19.004	.85	.15	1.897
3.5	.0302	.9698	19.396	.90	.10	2.302
4.0	.0183	.9817	19.634	.95	.05	2.995
4.5	.0111	.9889	19.778	.96	.04	3.220
5.0	.0067	.9933	19.866	.97	.03	3.500
5.5	.0041	.9959	19.918	.98	.02	3.910
6.0	.0025	.9975	19.950	.99	.01	4.600
7.0	.0009	.9991	19.982	—	—	—
8.0	.0003	.9997	19.994	—	—	—

may be rearranged to

$$A - W = Be^{-kt}$$

Then, taking natural logarithms on both sides,

$$\ln(A - W) = \ln B - kt$$

Solving for kt

$$kt = \ln B - \ln(A - W)$$

Then solving for age, t, we have

$$t = \frac{\ln B - \ln\,(A - W)}{k} \tag{16.12a}$$

which may be used directly for computing age, t, when any fraction of the mature weight is attained. By way of illustration, assume that it is desired to determine the age when

90 per cent of the mature weight is reached. The simplest procedure is to replace the W in equation (16.12a) by $0.9A$, obtaining

$$\begin{aligned} t &= \frac{\ln B - \ln (A - 0.9A)}{k} \\ &= \frac{\ln B - \ln 0.1A}{k} \end{aligned} \tag{16.12b}$$

from which evaluate t by substituting the numerical values for B, A, and k.

The above method for evaluating t for desired values of W/A is employed when one has growth equation (16.12) with its constant B. When one prefers growth equation (16.14), namely

$$W/A = 1 - e^{-k(t-t^*)} \tag{16.14}$$

the computation of t is carried out after rearranging to

$$1 - W/A = e^{-k(t-t^*)}$$

$$\ln (1 - W/A) = -k(t - t^*)$$

$$t = t^* - \frac{\ln (1 - W/A)}{k} \tag{16.14a}$$

As before, t is the age when a given fraction of the mature weight, W/A, is attained. The value of t is computed, as before, by substitution. Thus if it is desired to compute t when half the mature weight is reached, W is replaced by $0.5A$, obtaining:

$$t = t^* - \frac{1}{k} \ln 0.5 = t^* + \frac{0.69315}{k}$$

The labor of looking up natural logarithms in equation (16.14a) may be saved by the use of Table 19.2, which gives the values of $\ln (1 - W/A)$ for different values of W/A.

Table 19.3, giving the ages (from conception) at which different percentages of the mature weight are reached, was computed with the aid of equations (16.12a) and (16.14a), and they agree very satisfactorily with the values obtained by interpolation from the smoothed weight-age curves of the original data.[10]

Finally, Fig. 19.10 furnishes another graphic method for estimating the age at which a given percentage of mature weight is attained, from the value of the growth constant, k.

Summarizing, following the major inflection, the age curves of different species coincide on plotting W/A against $k(t - t^*)$. Physiological equivalence of growth in size may thus be estimated graphically or algebraically as explained in the text. The computation of this type of equivalence was made possible by the fact that, following the major inflection, the time rate of growth declines, in all cases, exponentially (at a constant percentage rate), or the mature weight, A, is approached in all cases at a constant percentage rate, k (as indicated by the equation $W = A - Be^{-kt}$). Only the numerical values of k differ; the *shape* of the curve is in all cases the same.

19.3: Age equivalence based on the proportionality between two biologically equivalent points. Pearl and Doering[11] superimposed the mortality age curves of three species so that two biologically equivalent points coincide. The equivalent points chosen were (1) the ages at which the specific death rate is minimum; (2) when but one survivor is left out of 1000 starting at age of minimum specific mortality. Their result, reproduced in Fig. 19.12, shows that the paths travelled by the age curves of the three species are different; hence equivalence for the intermediate age intervals is not satisfactory.

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[10] For the details of comparison see Brody, S., Univ. Mo. Agr. Exp. Sta. Res. Bull., 102, p. 17.

[11] Pearl, R., and Doering, C. R., *Science*, **57**, 209 (1923). Pearl and Parker, S. L., *Am. Naturalist*, **58**, 71 (1924).

Donaldson's[12] procedure of comparing age equivalence in man and rat on the assumption that 3 years in the rat is equivalent to 90 years in man is similar in principle to that of Pearl and subject to the same objection.

TABLE 19.2. To facilitate computing ages at which different fraction of mature weight, W/A, are reached

Fraction of mature weight (W/A)	$\ln(1 - W/A)$	Fraction of mature weight (W/A)	$\ln(1 - W/A)$
0.25	−0.28768	0.70	−1.2040
0.30	−0.35667	0.75	−1.3863
0.35	−0.43078	0.80	−1.6094
0.40	−0.51083	0.85	−1.8971
0.45	−0.59784	0.90	−2.3026
0.50	−0.69315	0.95	−2.9957
0.55	−0.79851	0.98	−3.9120
0.60	−0.91629	0.99	−4.6052
0.65	−1.0498	0.999	−6.9078

TABLE 19.3. Equivalence of Growth Age

Ages in months counted from conception when different percentages of the mature weight, A, are reached

(Computed from equation 16.14)

Percentage of mature weight, $100\frac{W}{A}$..	10	20	30	40	50	60	70	80	90	95	98	Mature Weight (kg)
1. Cow	10.6	13.1	16.0	19.4	23.4	28.2	34.5	43.3	58.4	73.4	93.2	550
2. Cow	11.2	13.6	16.2	19.3	23.0	27.4	33.2	41.3	55.1	69.0	87.3	460
3. Cow	10.9	13.1	15.5	18.4	21.8	25.9	31.2	38.7	51.6	64.3	81.4	420
4. Sow	5.9	7.9	10.1	12.7	15.7	19.5	24.3	31.0	42.4	53.9	67.3	200
5. Ewe	5.3	6.0	6.7	7.6	8.6	9.8	11.4	13.7	17.5	21.4	26.5	80
6. Guinea pig	2.8	3.4	3.9	4.5	5.3	6.3	7.5	9.3	12.3	15.4	18.9	0.825
7. White rat	2.2	2.4	2.6	2.8	3.1	3.5	3.9	4.5	5.6	6.7	8.1	.203
8. White rat	2.1	2.4	2.8	3.1	3.6	4.1	4.9	5.9	7.6	7.4	11.7	.280
9. White rat	2.0	2.4	2.8	3.2	3.4	4.4	5.2	6.3	8.4	10.0	12.9	.350
10. White mouse	.92	1.1	1.3	1.6	1.9	2.2	2.7	3.3	4.4	5.5	7.0	.0235
11. White mouse	1.1	1.2	1.3	1.5	1.8	2.0	2.3	2.8	3.7	4.6	5.6	.0275

1. Holstein (Eckles)
2. Ayrshire (Eckles)
3. Jersey (Eckles)
4. Duroc-Jersey (Mumford)
5. Suffolk (Murray)
6. Male (Wright)
7. Unmated female (Donaldson *et al.*)
8. Male (Donaldson *et al.*)
9. Male (Greenman and Duhring)
10. Female (Robertson)
11. Male (Robertson)

19.4: Pre-pubertal equivalence in weight growth. Preceding puberty the growth velocity, dW/dt, is proportional to (Sect. 16.4) the "effective weight",[13] W', so that the equation is

$$dW/dt = kW' = k(W + A) \tag{16.5a}$$

in which A is a constant. It may be interpreted to represent the weight equivalence of the growth impulse which, when added to the actual weight,

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[12] Donaldson, H. H., "Boas Anniversary Volume," New York, 1906.

[13] Weinbach, A. P., "The human growth curve," *Growth*, **5**, pp. 230 and 231 (1941).

w, transforms it into the "effective weight", W'. The integrated form of this equation is[13]

$$W = Be^{kt} - A = Ae^{k(t-t^*)} - A \qquad (16.5b)$$

which has the same form as equations (16.12) and (16.14). The equivalence for prepubertal age may, therefore, be determined in the same manner as the post-pubertal age. Weinbach has succeeded in preparing prepubertal-equivalence charts (Figs. 19.13a and 19.13b[13]).

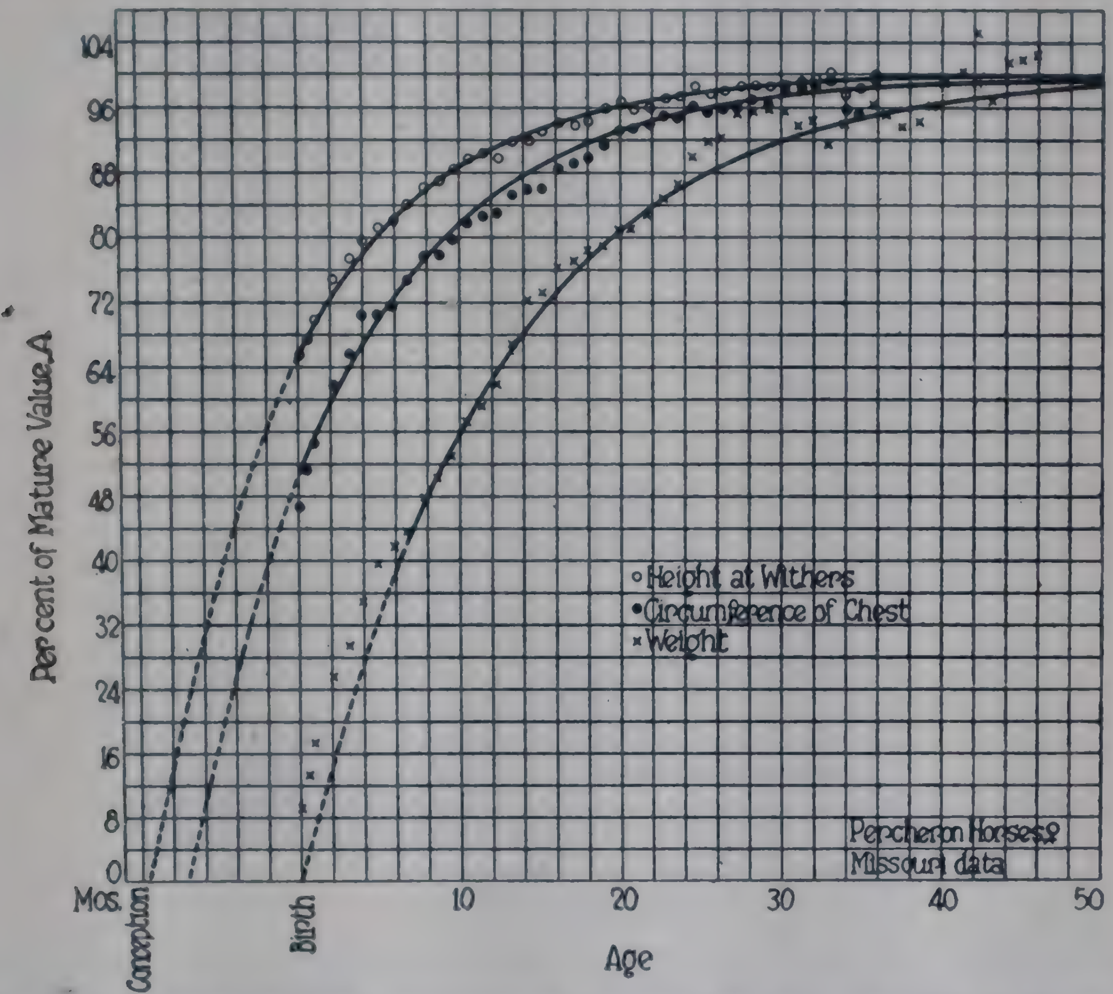

Fig. 19.35. Shows that each measurement approaches mature weight in horses at a different rate. The linearly-measured complexes approach mature size more rapidly than weight.

19.5: Senescence equivalence. Age equivalence with respect to senescence data (Ch. 18, generalized by an exponential equation $Y = Ae^{kt}$ or $Y = Ae^{-kt}$) may be evaluated by the same method as weight growth, employing the equivalent-time scale $k(t - t^*)$, in which k is the relative rate of senescence, and t^* is the age when the index of senescence is minimum.

Thus if the age change in specific mortality (deaths per 100 living of the same age) is taken as measure of age changes in senescence, the method consists[14] in plotting the ratios of specific mortality at age t to the minimum specific mortality, against the equivalence-time scale $k(t - t^*)$, in which t^* represents the age at minimum specific mortality, and k the relative increase in specific mortality per unit time, t, as explained in the preceding chapter. The results are shown in Figs. 19.14 and 19.15.

[14] Brody, S., *Growth*, **1**, 60 (1937), and Univ. Mo. Agr. Exp. Sta. Res. Bull., 105, 1927.

Interpretation of senescence-equivalence charts. Let us examine Fig. 19.15 to determine whether the population aged more rapidly when measured by rise in specific mortality from cancer or by rise in specific mortality from pneumonia.

The minimum mortality occurred at the same age, about 15 years, from both of these diseases. From Fig. 19.15, at age 15 years, the specific mortality was about 0.002 from cancer, and about 10 times as great, namely 0.02, from pneumonia; at age 70 years, the specific mortality was virtually the same, about 0.4, from both cancer and pneumonia. This means that the rise in the ratio, mortality at 70 years/mortality at 15 years, was much greater for cancer than for pneumonia. The *rise* in senescence, when measured by the *relative rise* in cancer mortality, is much steeper than when measured by the *relative rise* in pneumonia mortality.

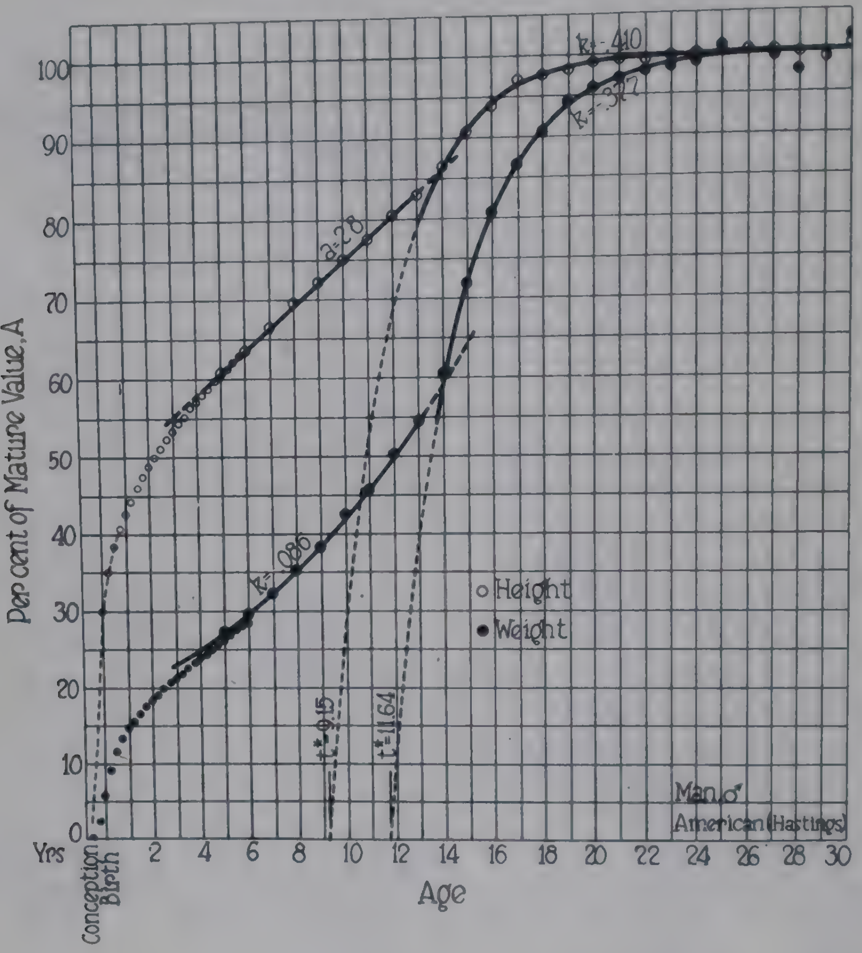

Fig. 19.36. Shows the relative rates of approach to mature height and weight in humans. Note differences and similarities between the weight and linear age curves of man and horse in the preceding figure. Incidentally, this chart indicates a method for predicting the future weight or height of a child. Thus, at age 9 years, the weight is 38 per cent of the maximum; hence a child weighing 23 kilograms at 9 years is likely to weight 23 × 100/38 = 60.5 kilograms at maturity. Similarly the weight at 12 years will be 60.5/2 = 30.3 kilograms, since a 12-year old child weighs 50 per cent of the mature weight. Or, since, a child weighs 23 kilograms or 38 per cent of mature weight at 9 years and 50 per cent at 12 years, therefore the weight at 12 years is 23 × 50/38 = 30.3 kg. The probable future height may be similarly estimated from this chart.

As shown in Fig. 19.14, this method of estimating senescence equivalence is also applicable to the rate of age change in egg production, healing of wounds, survival period of fibroblasts in blood serum from animals of different ages, or for any other exponential age change which may be taken as an index of aging.

19.6: Summary. A given chronological or physical time unit has a different physiological or functional significance for different organisms, for different organs in the same organism, at different ages, and under different conditions.

The rate of flow of physiologic time may be retarded or accelerated within certain limits. Thus in lower organisms, the flow of physiologic time may be practically stopped by desiccation.[15] But "growth time" may also be practically stopped in mammals, as illustrated in Fig. 19.16. Such experimental stoppage of "flow of time" is ordinarily dangerous (few animals survive this ordeal), but it illustrates dramatically the concept of the rate of flow of physiologic time and its manipulation by nutritional means.

Figs. 16.31, 16.32, and 19.17, 19.18 exhibit growth curves of rats maturing at different rates—that is, growth time flowing at different rates—because of difference in the nature of food supply. Fig 19.20 illustrates the relative rates of approach to mature weight of British children under different social-economic conditions (see also Figs. 16.33, 16.34 and 16.50 to 16.54). Are these differences genetic, environmental, or both? What is the effect of growth rate (approach to mature weight) on senescence rate? Fig. 19.21 exhibits the relative rates of approach to maturity with respect to total body weight, calcium, and phosphorus. Fig. 19.1 illustrates the influence of thyroid on the rate of growth.

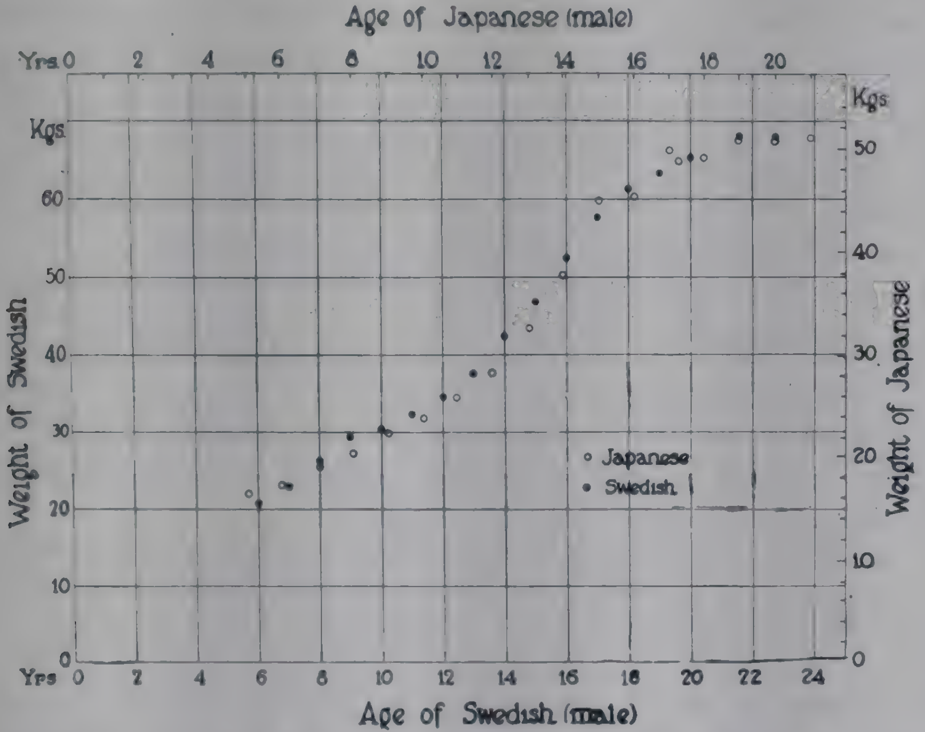

Fig. 19.37. Equivalence of age and weight of typical Nordic and Asiatic race.

While all organisms are alike in the shape of the growth curve following the major inflection, there are species differences in the ratios of the length of the segment preceding the major inflection to that following it. The growth curve of man is distinguished by a particularly long juvenile growth segment (3 to 13–16 years), a segment which is virtually absent in the other species examined (Figs. 16.6, 19.4, 19.5). This gives the growth curve of man a unique status with profound social, and especially educational, implications. Puberty in man occurs very late in the growth history, when about $\frac{2}{3}$ of the mature weight is achieved, whereas in the other species it occurs when about $\frac{1}{3}$ of the mature weight is reached (Fig. 16.6). One of the unique characistics of the human family, the simultaneous presence of dependent children of different ages, is based on this relatively long pre-pubertal period. The mechanism, probably endocrine in nature, involved in this unique delay of puberty in man is one of great interest.

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[15] Conklin, E. G., *Popular Science Monthly*, **83**, 197 (1913).

An important aspect from the growth-efficiency viewpoint is that animals differing in mature weight may reach maturity in the same time. Thus (Fig. 19.22), the Flemish rabbit is over twice as large as the Polish rabbit, yet both reach maturity in the same time. Obviously the gains in the larger rabbit are made more efficiently (and more profitably) than in the smaller. Likewise, rat, dove, and pigeon are in the same weight class (Fig. 16.48), yet pigeon and dove approach mature weight more rapidly than the rat (Figs. 16.48 and 19.24). What are the mechanisms controlling these peculiar differences in the rates of approach to mature weight?

Some of the technically useful features of this chapter are: methods of computing age equivalence in animals, plants, and populations; demonstrating simlarities between the age curves of animals, plants, and populations; interpreting experimental results obtained on one species, such as rats or rabbits, in terms of other species, such as cattle or human beings, for physiologically equivalent age and time intervals.

Many equivalent charts are also presented in Chapter 16. See especially Figs. 16.6, comparing the age curves of growth of rat, yeast *population*, maize, oat, squash; 16.7, curves of man, cattle, swine, sheep, rabbit, fowls, rats, guinea pigs, pigeons; Figs. 16.35 to 16.38, equivalence of age for milk secretion in cattle; Figs. 16.30 and 16.32, remarkable differences in rate of approach to mature weight in rats. Additional equivalence charts, not discussed in the text, are presented because of their inherent interest and usefulnes as references or standards for evaluating equivalence of growth age in different species and breeds of farm and laboratory animals.

The sources of data are indicated on the chart, the references are in the legends, or in Chapter 16; also in University of Missouri Agr. Exp. Sta. Res. Bull. 96.

Chapter 20

Nutritional Aspects in the Efficiency Complex

> The scientist works in his laboratory with a few pink-eyed rats, and what he discovers is seen to be tied in with the deepest social and political and economic problems. *Gove Hambidge*

> Tell me what you eat and I will tell you what you are. The destiny of a people depends on the nature of its diet. *A. Brillat-Savarin* (1755–1826)

20.1. Introduction: Species and individual differences in dependence on food for vitamins and amino acids. Every chapter in this book is concerned with some nutritional problem. This chapter considers several nutritional aspects as a whole, from the organismic viewpoint, with special reference to problems engaging students of practical nutrition of animals and man.

The nutrition of higher animals involves many nutrients, usually grouped into four broad categories: (1) protein or amino acid, (2) energy (which includes protein as well as carbohydrate and fat), (3) mineral or inorganic, (4) vitamin. There are, however, many species and even individual peculiarities with respect to the degree of dependence on food for each of the many nutrients included in these four categories.

For instance, most microorganisms, such as yeast, can synthesize amino acids and protein from simple compounds, such as asparagin, urea, succinamide, nitrites, nitrates, and ammonium bicarbonate. Higher animals, on the other hand, cannot synthesize what are called "nutritionally essential" amino acids. Yet ruminants, such as cattle and sheep, are not entirely dependent on their feed for the amino acids because one of their stomach chambers, the rumen or paunch, is virtually a fermentation vat with flourishing populations of microorganisms which convert simple non-amino-acid nitrogen compounds into amino acids for the synthesis of their body protein; these microorganismal-body proteins are in turn used as food by their host, the ruminant animal. It thus comes about that ruminants convert inferior proteins and even non-protein nitrogen compounds into superior proteins in milk and meat, which non-ruminants cannot do. Ruminants, especially dairy cattle, thus occupy a unique position in the efficiency complex in that they can convert feeds, with much crude roughage not useful to man and other species, and inferior protein or non-protein nitrogen compounds into the very best proteins, meat and milk. Swine and poultry may be efficient converters of feed into meat or eggs, but the feed has to be concentrate rather than roughage, and the protein must contain all the essential amino acids and vitamins.

It is evident that the concept "biologic value" of protein (page 778), applicable to species with simple stomachs, such as rats[1], pigs[2], or chickens[3], which are dependent exclusively on their diet for essential amino acids, is not applicable to ruminants[4]. Urea and casein, for example, when fed to ruminants as supplements to a low-protein ration yield virtually the same protein-utilization values. Results on the biologic value of protein obtained on rats or even rabbits are not, therefore, applicable to ruminants. Digestibility, not "biologic value" of the dietary protein is the major factor in evaluating protein for ruminants. It was formerly thought desirable to prepare complex grain mixes for dairy cattle on the assumption that the greater the variety the more likely is the mix to contain all the amino acids for synthesis of milk protein. This idea is now outmoded. It is now believed that one grain is as good as a mix of many[5] if equally digestible and palatable (Fig. 20.4).

What was said about microbiological synthesis of essential amino acids in the rumen holds even more conclusively for microbiological synthesis of the B-complex vitamins (Ch. 6) in the rumen.

This has been demonstrated by *in vivo* (fistula) and *in vitro* (after slaughter) methods as well as by feeding experiments. Synthesis in the rumen was observed of thiamine, riboflavin, pyridoxine, nicotinic acid, biotin and pantothenic acid[6]. Ruminants, such as cattle, sheep, and goats, are thus not dependent on dietary water-soluble vitamins, nor on vitamin K. This fact is of immense national economic importance, permitting the production of the "almost perfect food", cow's milk, from feeds which are poor in protein and B-vitamins.

These statements about microbiological synthesis do not, of course, apply to calves prior to their development of the rumen function. In this condition they need dietary vitamins as do other species[7].

Normally ruminants do not need dietary ascorbic acid. However, the rate of its synthesis seems to depend on the vitamin A intake[7], age[8], and general condition[8]. (The rate of ascorbic acid synthesis in non-ruminants also depends on thiamine supply[9].)

Ruminants, of course, need dietary vitamin A, which they obtain in carotene form from green roughage.

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[1] Kriss, M., and Marcy, L. F., *J. Nut.*, **19**, 141 (1940).

[2] Moore, D. D., *et al.*, *J. Biol. Chem.*, **91**, 373 (1931).

[3] Rice, C. M., and Dean, L. A., *Poultry Sci.*, **21**, 15 (1942).

[4] Swanson, E. W., and Herman, H. A., Univ. Missouri Agr. Exp. Sta. Res. Bull. 372, 1943 (extensive review). Salisbury, G. W., and Morrison, F. B., *J. Dairy Sci.*, **21**, 106 (1938). Bartlett, S., *J. Dairy Res.*, **9**, 263 (1938). Hart, E. B., *et al.*, *J. Dairy Sci.*, **22**, 785 (1939); **23**, 123 (1940); **24**, 51, 835 (1941). Miller, J. I., and Morrison, F. B., *J. Agr. Res.*, **65**, 429 (1942). Mitchell, H. H., *et al.*, *J. Nut.*, **22**, 167, 183 (1941); *J. Animal Sci.*, **1**, 236 (1942). Harris, L. E., *et al.*, *Id.*, **2**, 328 (1943). For reviews of the older literature on urea utilization, see Armsby, H. P., "The nutrition of farm animals", Macmillan, 1917; Mitchell, H. H., and Hamilton, T. S., "The biochemistry of amino acids", Reinhold Pub. Corp., pp. 571–88, 1929.

[5] Dawson, J. R., *et al.*, "Single grain and grain mixtures as supplements to alfalfa hay and silage for milk production", U. S. Dept. Agr. Circ. 696, 1944.

[6] Goss, H., *Nut. Abstr. Rev.*, **12**, 531 (1943) (extensive review). McElroy, L. W., and Goss, H., *J. Nut.*, **20**, 427, 541 (1940). Wegner, M. I., *et al.*, *Proc. Soc. Exp. Biol. Med.*, **45**, 769 (1940); **47**, 90 (1941). Hunt, C. H., *et al.*, *J. Nut.*, **21**, 85 (1941). Savage, E. S., and McCay, C. M., *J. Dairy Sci.*, **25**, 595 (1942). Lardinois, C. C., *et al.*, *Id.*, **27**, 579 (1944).

[7] Sutton, T. S., *et al.*, *J. Biol. Chem.*, **144**, 183 (1942).

[8] Phillips, P. H., *et al.*, *J. Dairy Sci.*, **24**, 153 (1941).

[9] Govier, W. M., *Science*, **98**, 216 (1943).

The other species of farm animals do not have such "fermentation vats" in their stomachs, and the microorganisms in the intestine are relatively few and relatively useless for the purpose of synthesizing amino acids and vitamins. Moreover, the absorption from the lower part of the intestine is inefficient. The simpler the digestive tract the less the opportunity for synthesis of amino acids and vitamins by microorganisms and the greater the dependence on dietary nutrients, although, it is certain that, variable amounts of synthesis occur in all species[9a], even in humans[72], which explains, in part, species and individual variations in sensitiveness to withholding dietary vitamins of the B complex. Biosynthesis has been demonstrated in the rat cecum[10a].

Anthropoids—including man—and guinea pigs are dependent not only for the B vitamins but also for ascorbic acid (vitamin C) in their food. The farm and laboratory animals investigated synthesize ascorbic acid (Ch. 6).

Ruminants, then, are least likely to develop nutritional deficiencies, being able to synthesize essential amino acids (within limits) and the B-complex vitamins and vitamin K. These are followed, as a rule, but with many exceptions, by the non-ruminant herbivors; then by omnivors, such as swine and poultry, which have still simpler digestive tracts, cannot consume much roughage, and which therefore frequently develop nutritional deficiencies under intensive commercial conditions of management. Grass, properly cured early-cut hay, and other young leafy greens are "protective foods," and the less their consumption the greater the chances for developing dietary deficiencies. Fourth, are such species as rats and dogs which do not normally consume appreciable quantities of greens and are, therefore, still more likely to develop nutritional deficiencies. The anthropoids, including man, come in the last category; they are, in a sense, the most exacting in their food needs because in addition to the vitamins needed by the other species, they are also dependent on their food for vitamin C and for unknown factors[10].

It is, then, evident that in addition to the four broad categories of energy, nitrogen, minerals, and vitamins, which all animals must have, each species and even each individual has special dietary needs not necessarily applicable to other species and individuals. It is necessary to appreciate the lability of need in the same individual (with age and other conditions) and the differences between species and individuals in order to interpret apparently contradictory experimental results. Moreover, different species vary in their response to dietary situations. A dramatic example of this is furnished by the differences between the large fertile queen bee and her small infertile sister worker bee. This difference is developed by dietary means alone, by feeding "royal jelly" to the larva of the future queen but (following the third day) not to the future worker bee.

[9a] Mitchell, H. K., Taylor, A., *et al.*, Univ. Texas. Pub. 4237, 1942.

[10a] Guerrant, N. B., and Dutcher, R. A., *Proc. Soc. Exp. Biol. Med.*, 31, 796 (1934).

[10] Waisman, H. A., *et al.*, "Nutritional needs of the monkey," *J. Nut.*, 26, 205, 361 (1943).

Nothing is known about the composition of "royal jelly" to indicate the nature of its growth and differentiating properties[11a]. The worker bee is apparently not underfed or malnourished. The worker bee is not analogous, for example, to a vertebrate cretin produced by dietary iodine deficiency. The queen bee appears to be (qualitatively and quantitatively) superfed. It is doubtful whether such striking developmental differences can be achieved by superfeeding normally fed mammals and birds (Ch. 16). It may be that "royal jelly" contains not only what are usually called nutrients, but also hormones since, unlike the food of worker bees, it is a secretion and there is apparently no digestion in the queen bee to destroy hormones. If "royal jelly" contains hormones, its feeding may be analogous to injecting anterior pituitary growth hormones (Sect. 7.7).

Nutritional investigation includes many specialties, ranging from comparative nutritional psychology concerned with individual differences in food preferences to organic chemistry concerned with the identification and synthesis of nutrients; from sociology concerned with interrelation between diet and social and national welfare to physical chemistry concerned with the thermodynamics, time relations, catalysts, and other physico-chemical reactions constituting life. This chapter, naturally, makes no attempt to cover the field of nutrition but discusses several selected problems which seem germane to the spirit of this book. One of the problems, species and individual differences in dependence on food for vitamins and amino acids, and species differences in response to superfeeding, is discussed in this introductory section. The following section discusses species and individual differences in the use of what may be called "nutritional wisdom" in the choice of dietary components.

20.2. "Nutritional wisdom." It is fascinating to watch individual rats, chickens, children (and also the children's parents) making up their own ration, each to his unique taste, when a wide variety of foods is available *ad libitum* in cafeteria style. Individuals undoubtedly differ in food preferences; when followed, these preferences affect the individual's well being. This is illustrated, for example, by developmental differences of the animals described by Dove which were allowed to make their own ration.[11]

If an animal chooses consistently a dietary pattern that leads to optimal growth, health, and longevity, then, conversely, the dietary pattern chosen by such an animal may indicate the proportions between the foods that lead to optimal growth, health, and longevity. Foods may this way, with the aid of superior assay animals, be arranged in a hierarchal order in terms of "palatability ratings." Palatability is an agriculturally important characteristic because the greater the palatability of a food the greater its consumption, the more rapid the productive process, the less the overhead maintenance cost, and the higher the economy per unit product (Ch. 1).

Dove[12] employed this method of self-selection for arranging foods by their palatability. When offered free choice of the following foods to rabbits between weaning and 11 weeks, they consumed 36 per cent whole-ground wheat, 21 per cent whole-ground yellow corn (mixed with 1 per cent cod liver oil), 18 per cent dried skim milk, 8 per cent whole-ground oats, 8 per cent alfalfa leaf meal, 3 per cent dehydrated fishmeal, 2.3 per cent meat meal, 1 per cent common salt, and 1 per cent bone meal.

[11a] Pearson [*Proc. Soc. Exp. Biol. Med.*, **48**, 415 (1941)] reported that "royal jelly" is very rich in pantothenic acid.

[11] Dove, W. F., *J. Heredity*, **30**, 157 (1939), and other references (ref. 17, Ch. 1).

[12] Dove, W. F., *J. Nut.*, **25**, 447 (1943); *Human Biology*, **15**, 199 (1943).

Dove[12] also observed that rabbits give highest preference to succulent foods with highest moisture and lowest fiber content. For instance, cabbage with the highest (96%) moisture and lowest (1%) fiber content in the succulent test foods was given highest preference, while white sweet clover before bloom with the lowest (75%) moisture and highest (6%) fiber content was given the lowest preference. Since high moisture and low fiber content are correlated with physiological immaturity and with the associated "tenderness" or high digestibility and high vitamin-mineral content, the rabbit's preference is essentially for the most digestible foods richest in vitamins and minerals, a preference that accords with "nutritional wisdom".

What was said concerning normal food choice often holds for "cravings" during certain nutritional disorders and under special stressful conditions. Such kinds and amounts of foods are generally sought as will restore and maintain a normal nutritional state. This accords with the principle of homeostasis (Ch. 10); and under natural conditions appetite for *natural* foods is an important guide to the nutritional needs of the body[13]. (Conditioned appetite for artificial foods or condiments, such as for sugar, patent flour, alcohol, etc., obviously belongs in a different category of wants.)

For instance, during a certain disease of the adrenal glands associated with extreme loss of common salt (Sect. 7.4), the animal automatically (under the influence of taste-hunger mechanisms) compensates the salt loss by developing an "abnormal" craving for and consuming enormous quantities of table salt[14]. Indeed, extreme salt consumption is often taken as a diagnostic symptom of such adrenal disease. Similarly[15], removal of the parathyroids (which regulate calcium metabolism, see Sect. 7.5) is associated with a craving for and four-fold consumption of calcium; and conversely, unusual craving for bone or earth (in non-lactating and non-gestating animals) may indicate parathyroid abnormality. Another example relates to craving for unusual foods during pregnancy and lactation, as illustrated by bone consumption in herbivors (that do not normally consume animal products) during gestation and lactation when there is heavy demand for calcium[16]. There is also an increased need for protein, but not carbohydrate, during pregnancy, and pregnant rats fed by the self-selection method increase their protein, but not carbohydrate, intake[17].

Some types of cravings associated with disease, such as sugar craving by diabetics, when satisfied, may aggravate the disease.

Carbohydrate and protein oxidation (catabolism) in normal manner is dependent on the presence of thiamine catalysts (Ch. 6); and interestingly enough the relative preference by rats for carbohydrate and fat depends on the relative supply of thiamine; its lack leads to aversion to carbohydrate and increased preference for fat and also for yeast (rich in thiamine); its abundance changes the preference from fat to that of carbohydrate[18]. This "nutritional wisdom" relating to thiamine does not, apparently, extend to riboflavin. Chickens[19] and rats[20] do not differentiate satisfactorily between riboflavin-poor and riboflavin-rich diets even if they suffer seriously from riboflavin deficiency.

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[13] Mitchell, Helen S., and Mendel, L. B., "The choice between adequate and inadequate diets as made by rats and mice", *Am. J. Physiol.*, **58**, 211 (1921).

[14] Richter, C. P., *Endocrinology*, **22**, 214 (1938); **24**, 367 (1939); *Am. J. Physiol.*, **126**, 1 (1939). Swann, H. G., *Science*, **90**, 67 (1939).

[15] Richter and Eckert, J. F., *Endocrinology*, **21**, 50 (1937).

[16] Green, H. H., "Preverted appetites", *Physiol. Rev.*, **5**, 336 (1925). Carlson, A. J., "Bone eating by the pregnant and lactating squirrel", *Science*, **91**, 573 (1940).

[17] Richter, C. P., *et al.*, *Am. J. Physiol.*, **124**, 596 (1938).

[18] Richter and Barleare, B., *Am. J. Physiol.*, **127**, 199 (1939).

[19] Jukes, C. L., *J. Comp. Psychol.*, **26**, 135 (1938).

[20] Harris, L. J., *et al.*, *Proc. Roy. Soc.*, **113B** (1933).

Chicks balance their rations satisfactorily from natural feeds, as indicated by the following comparison at the Missouri Experiment Station[21] between the free-choice (cafeteria) selection of chicks up to 8 weeks of age and the chick mash officially recommended by the Missouri Station.

Feed Consumption by Chicks During the First 8 Weeks After Hatching.

Feed	Free selection (%)	Recommended Missouri ration (%)
Cornmeal	39	50
Wheat shorts	29	15
Wheat bran	11	15
Dried buttermilk or	6	15
Dried skim milk	5	15
Meat scrap	5	0
Bone meal	3	4
Alfalfa leaf meal	1	0
Salt	0.2	1

The above self-selected ration contains about 18 per cent protein, 56 per cent carbohydrate, 4.7 per cent fat, 7.1 per cent ash, and 3.5 per cent crude fiber.

Commercially managed dairy cattle do not seem to be particularly endowed with nutritional wisdom[22]; they tend to overeat, sometimes on one feed then on another, without apparent "reason".

If unconditioned weaning children[23] are given the opportunity to choose their food constituents, their choice is satisfactory. However, children are rarely unconditioned even before weaning and real free choice, in the sense of freedom from habit and suggestion, is perhaps impossible; therefore, conclusions from children's self-selective behavior are usually ambiguous.

Human choice of food is particularly confused by the more rapid advances in the technology of food processing than by the understanding of the nutritional significance of the processing. This lag of understanding behind technological skill leads to the development of irrational ideas and undesirable habits surprisingly difficult to eradicate when understanding does catch up with technology. A few examples with their social implications are cited in the following notes to illustrate this point.

Bread is the major food stuff, the common man's "staff of life". It is a good food if made from whole grain, as it contains good proteins, minerals, and vitamins. Until recently whole grain was used for bread making. But recently technology was developed for processing whole-wheat into "patent flour" which has very fine *culinary* qualities, making a "lovely crust" and a "big loaf" (per unit weight of flour). *Nu-*

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[21] Funk, E. M., *Poultry Sci.*, 11, 94 (1932). For self-selection by laying hens, see Kempster, H. L., *Id.*, 3, 26 (1916), and Rugg, W. C., Austral. Dept. Agr. Bull. 54, 1925. Amon, V. G., *Phillip. Agriculturist*, 19, 445 (1930). The self-selection is nutritionally very satisfactory.

[22] Nevens, W. B., *J. Dairy Sci.*, 2, 435 (1919); Univ. Ill. Agr. Exp. Sta. Bull. 289, 1927. For water drinking, see Atkeson, F. W., and Warren, T. R., "Water consumption in dairy cows", *J. Dairy Sci.*, 17, 265 (1934).

[23] Davis, C. M., "Self-selection of diet by newly weaned infants", *Am. J. Dis. Child.*, 36, 651 (1926); 46, 743 (1933). Harris, L. J., *British Med. J.*, 2, 309, 367 (1933).

tritionally, however, the patent flour is very inferior to the whole-wheat flour because the milling process removes the nutritionally superior proteins and, roughly speaking, $\frac{3}{4}$ of the iron, $\frac{1}{2}$ of the calcium, $\frac{3}{4}$ of the copper, $\frac{3}{4}$ of the thiamine, $\frac{3}{4}$ of the riboflavin, $\frac{1}{2}$ of the choline, and nearly all the magnesium and manganese, leaving the patent flour a nutritionally impoverished product. The superior keeping quality of white flour is due mostly to these very nutritional deficiencies which make it an unfavorable diet for the pests (which thrive on the nutritionally superior whole-wheat flour).

The germ, middlings, shorts, red dog flour, and bran (Fig. 20.1) removed from the wheat in white flour manufacture[24], which carry the vitamins, superior proteins, and minerals, are fed mostly to cattle. But, as previously explained, cattle are independent of dietary B vitamins and essential amino acids, and they obtain minerals from the roughage and bone meal. We thus take away from the human dietary what man needs and feed to cattle what cattle do not need, which does not make particularly good "nutritional wisdom", or even horse sense. It has been said that white-flour products and sugar[25] furnish over half of the calories, but only 10 per cent of the vitamins and minerals. The milling also disturbs the supplementary balance between amino acid in the various parts of the grain[26], thus converting a naturally balanced protein combination into an unbalanced one.

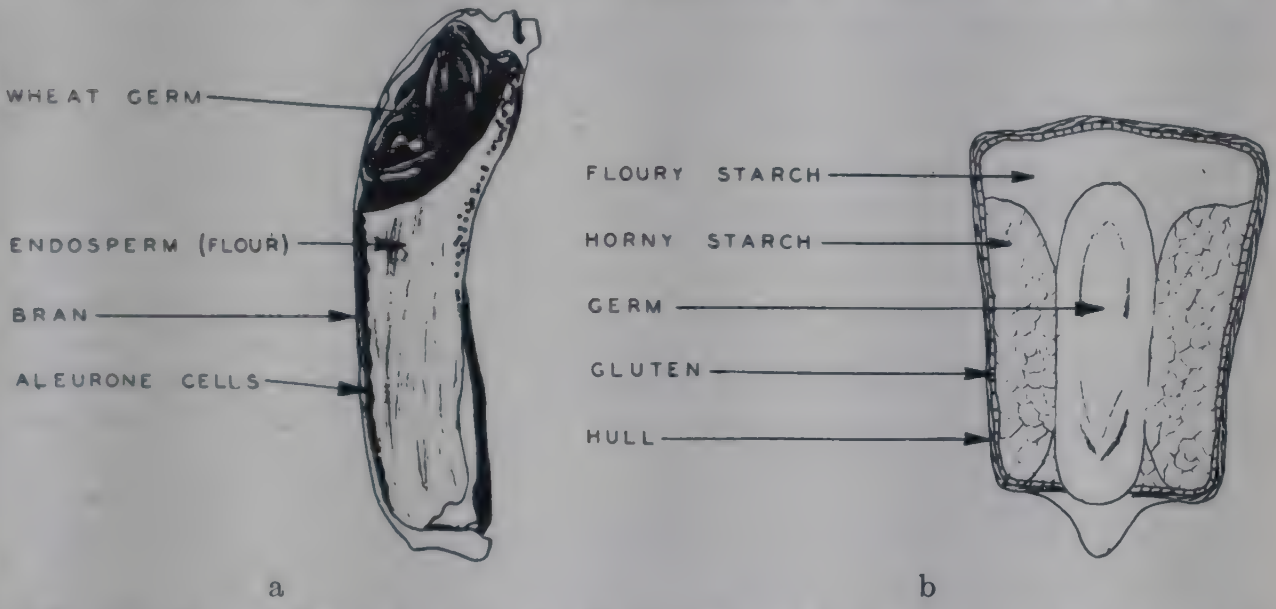

Fig. 20.1a and b. Wheat and corn grains. The wheat grain consists of about 1.5 per cent germ or embryo (which contains about 40 per cent of the whole-grain protein and 15 per cent of the vitamins), 15 per cent bran and inner coatings (which hold about 18 per cent of the whole-grain protein and 75 per cent of the B vitamins), 83 per cent endosperm (which contains about 11 per cent of the whole-grain protein and 10 per cent of the vitamins). Patent flour consists mostly of endosperm. Middlings or shorts is a mixture of some bran, some germ, and some red dog flour; red dog flour or white middlings consists chiefly of aleurone cells with some bran and flour particles. Middlings, the most nutritious part of the wheat, a very rich source of the vitamin B complex, is now fed to livestock.

Next to bread, milk is—or should be—the most important article of diet for the common man because it is the most efficiently produced, as above explained, and it is the least expensive protective food of animal origin (Ch. 21). Milk is rich in protein of the highest quality, minerals, vitamins, and the unique milk sugar. But after producing, about half of it is skimmed and the milk under the cream line is fed to farm livestock which convert the milk to other products (egg, meat, meat fat) at an overall efficiency of, perhaps, 10 per cent (Sect. 21.2). According to a recent report[27] "Less than half the available milk protein finds its way into the human diet . . . one can scarcely condone the lavish waste of nutritious materials now occurring annually in the dairy industry. The full significance of this incredible situation is appreciated when one realizes that the milk protein remaining on the farms each year is equivalent to the protein content of 20 million beef steers . . ." (Further analysis of the nutritional and social implications of processing wheat and milk, and the relation between the two, are presented in Sect. 21.2.)

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[24] For cereal chemistry consult the *Journal of Cereal Chemistry*; Stanford University Food Research Studies; Bailey, C. H., "Constituents of wheat and wheat products", Reinhold Pub. Corp., 1944; Sherman, H. C., "Modern Bread", Macmillan, 1942.

[25] Sugar, which, like alcohol, should be used as flavoring material and *apéritif*, has become a major article of the dietary. A century ago the per capita sugar consumption was 8 lbs per year; in 1941 it was 112 lbs per year (Sect-21.2).

[26] Chick, Hariette, *Lancet*, **1**, 405 (1942). Murlin, J. R., *et al.*, *J. Nut.*, **22**, 573, 589 (1941).

This complex sequence of processing and reprocessing gives the impression that man is employing his ingenuity for devising complex methods for wasting food.

The "enrichment" of patent flour with vitamins does *not* compensate for the losses in milling, as indicated by short-time observations on dogs and rats on whole-grain and "enriched" white flour[28]. The "enriched" bread is deficient in the amino acids lysine and valine, as well as in vitamins and minerals and unknown factors. Long-time experiment would, no doubt, bring out many other deficiencies. The Nutrition Committee of the National Health and Medical Research Council of Australia rejected the principle of bread "enrichment" with vitamin B complex[29], preferring to add cereal by-product, such as wheat germ, to the white flour or dried milk, and war-time, Britain compels the use of but lightly extracted "national wheat meal"[30].

Incidentally, oatmeal or rolled oats, nutritionally considered, is a whole grain rather than a milled one, like decorticated wheat, and is much richer in vitamins, minerals, protein, and fat then even whole wheat.

The least expensive, yet the best substitute for the losses incurred in milling wheat is non-fat milk solids added to the extent of 6 per cent of the white flour. Indeed, according to Mitchell[28], who employed growth rate of immature rats as a measure of nutritional value of bread, skim-milk solid is a better supplement to white flour than the wheat residues discarded in milling, and such milk addition definitely improves the nutritive value both of "enriched" white bread and whole-wheat bread. The ideal, nutritionally complete bread would be made from whole wheat and whole milk. With the exception of ascorbic acid, a bread made from whole-wheat flour and whole milk would constitute a nutritionally complete diet (Sects. 21.2 and 18.2.4), although rather low in vitamin A.

White flour would also be greatly improved in nutritive value by supplementing it with such vitamin-rich and protein-rich foods as yeast, soybean flour, peanut flour, wheat germ, and so on. Aside from its nutritionally supplementary value, 3 to 10 per cent soybean flour mixed with white wheat flour makes an unusually attractive bread crust and holds moisture, thereby increasing the keeping quality of the bread.

The economically able who are also equipped with nutritional knowledge may, of course, compensate the white-flour deficiencies with appropriate protein-mineral-vitamin-rich foods—milk, eggs, meat, fresh vegetables, fruits. But most consumers lack both means and knowledge for correcting the white-flour deficiencies; hence the importance of an inexpensive "national loaf" which would supply the majority of consumers all the nutritional essentials (Sect. 21.2). The modern large-scale bakeries and their cooperative institutes are in a position to experiment in blending various types of flours, milk solids, yeast, lecithin, agar, and so on, with the aim of developing both an attractive and nutritionally complete bread, and there is no doubt that they will live up to this opportunity.

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[27] Rose, W. C., *et al.*, "The nation's protein supply", report of Food and Nutrition Board, National Research Council, Circ. 114, 1942.

[28] Murlin, J. R., *Am. Soc. Exp. Biol., Fed. Proc.*, **1**, 209 (1942). Light, R. F., and Frey, C. N., *Cereal Chemistry*, **20**, 645 (1943). Mitchell, H. H., *et al.*, *J. Nut.*, **25**, 585 (1943). Higgins, G. M., *et al.*, *Id.*, **26**, 347 (1943).

[29] Anon., *J. Am. Med. Assn.*, **116**, 882 (1941), and **126**, 315 (1944).

[30] Blainey, A., *Nature*, **152**, 191 (1943).

What has been said about the losses in grain processing applies to other foods as well. For instance, we have an abundance of efficiently produced inexpensive vegetable fats. The keeping qualities and decomposition temperatures of these fats (natural and hydrogenated) are approximately the same as of lard; yet lard has been produced on a large scale at an energetic efficiency below 10 per cent of that of vegetable fat and at a high nitrogen and mineral cost. There are good reasons for lard as for patent flour production, but the reasons are not from the overall national nutritional efficiency viewpoint (Ch. 1). This fact is becoming evident and efforts are already being made to develop a non-lard type of swine.

Some of the oil-bearing legumes, especially soybeans, are efficient protein as well as fat producers[31], and the soybean promises to become a most important food crop in this country[32, 33].

Fish has approximately the same nutritional value for man as meat (except for iron), and it is said to be obtained by the fishing industry at a man-power cost of about one-tenth that of meat[33]. But relatively little fish is used as human food in this country. After removing the oil, most of the commercial catch is used for animal feed or even fertilizer.

Yeast is one of the richest sources of the B-complex vitamins and protein of high biologic value, and the raw material for yeast manufacture (molasses, and more recently waste sulfite liquor) is plentiful. The nutritive value of yeast is quite close to that of lean meat of the same water content. Little yeast, however, is being used for human consumption. Attention is now given to yeast culture as human food[33, 34]. Yeast, like soybean flour or milk, could be incorporated in bread up to, perhaps, 10 per cent, thereby enriching the bread with vitamins and proteins; or, like milk and soybean, yeast could be used for the preparation of very rich protein-mineral-vitamin soups to supplement the perverted white flour-sweets diet (Sect. 21.2).

While discussing yeast, a relatively new article in the human dietary, one may mention another new product with potentialities for supplementing the human dietary, namely dehydrated young cereal grass[35]. Young tender grass (harvested just before the jointing stage, about 3 weeks after seeding under favorable weather conditions) is rich in all essential nutrients and also in pectin and chlorophyll, which exert a hygienic effect on the digestive tract. Such grass constitutes a great reservoir of vitamins, proteins, and minerals. Grass, when young and tender, can be consumed in but limited amounts because of its laxative effect which, however, judging by the huge sale of laxatives, is also an advantage. Here is a problem in processing which may yield a matchless dietary constituent from a heretofore untapped resource (see page 789).

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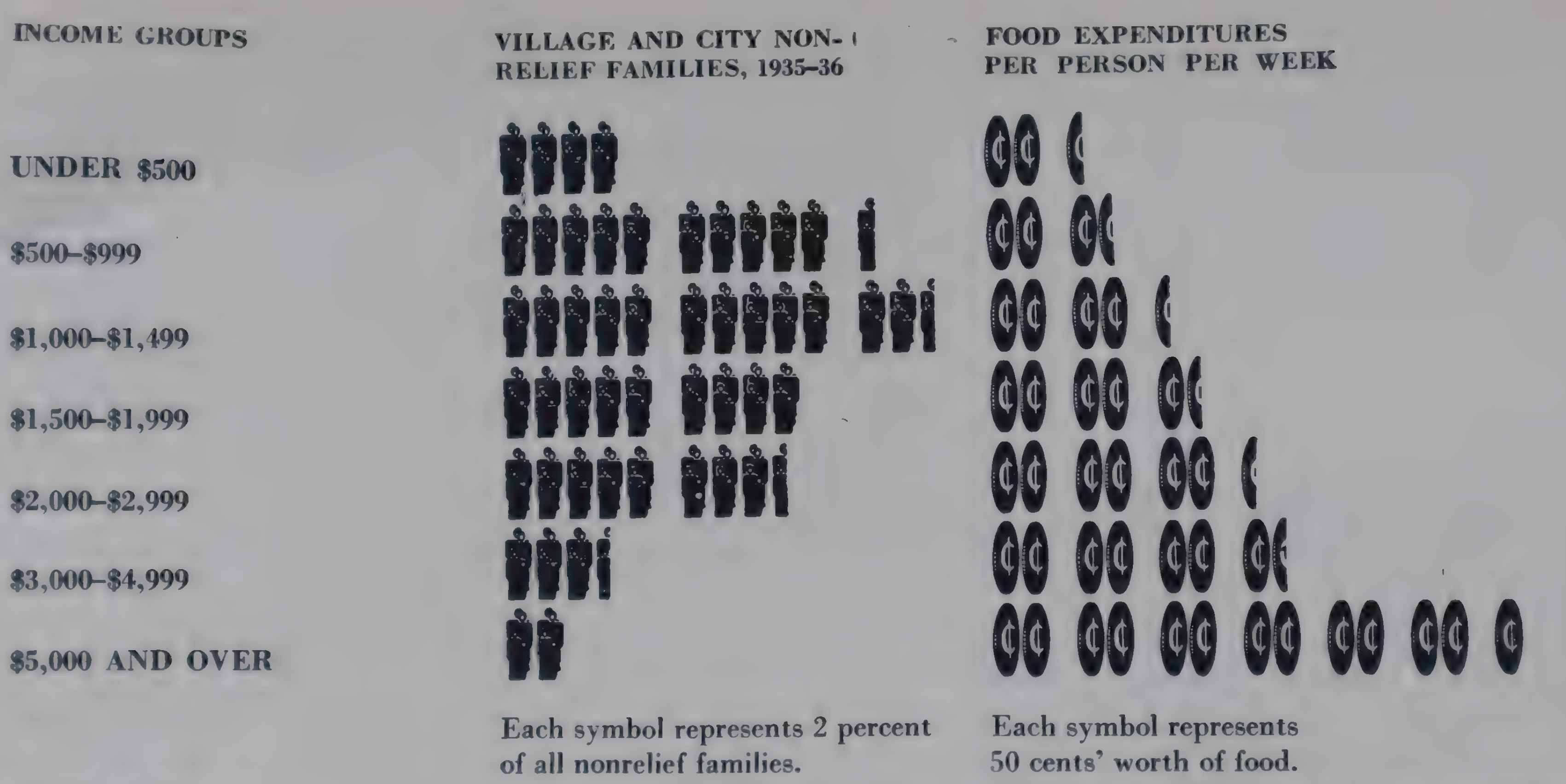
[31] Rose, *et al.*[27], Stare, F. J., and Hegsted, D. M., "Special report on protein foods", National Research Council, 1943.

[32] Baldwin, I. M., and Movitt, E. J., *Food Res.*, **7**, 403 (1943). Burkholder, P. R., "Vitamins in soybeans", *Science*, **98**, 188 (1943). See also "The composition and nutritive properties of soybean products" by the Soybean Nutrition Research Council, Chicago, 1938. The literature on soybeans is too large for detailed citation

[33] Frey, C. N., "History of the yeast industry", *Ind. Eng. Chem.*, **22**, 1148 (1930). Gortner, R. A., Jr., and Gunderson, F. L., *Chem. Eng. News*, **22**, 160 (1944).

[34] Thaysen, A. C., *Nature*, **151**, 406 (1943). Burton, L. V., *Food Ind.*, **15**, 66 (1943). Macroe, R. F., *Bioc. J.*, **36**, 460 (1942).

[35] Schnabel, C. F., *Abst. Div. Biol. Chem., Am. Chem. Soc., N. Y.*, 1935. Kohler, G. O., *J. Biol. Chem.*, **152**, 215 (1944). For weeds as food, see Carver, George W., "Nature's garden", Tuskegee Institute, Alabama, Bull **43**, 1942.



SOME OF THE FOODS THEY HAD		THESE ARE THE QUANTITIES EACH PERSON HAD IN A WEEK		
		$1.75 group	$3.15 group	$4.55 group
MILK (OR ITS EQUIVALENT)	pints	4	7	9
EGGS	number	3	5	8
MEATS, POULTRY, FISH	pounds	1½	2½	3½
TOMATOES, CITRUS FRUITS	pounds	1	1½	3
LEAFY, GREEN, AND YELLOW VEGETABLES	pounds	1	1½	2

Fig. 20.2. The relation between monetary income, expenditures for food, and consumption of protective foods (re-arranged from Stiebeling[37]), indicating that malnutrition is a problem in dollars and cents as well as in proteins, vitamins, and minerals.

The waste, or failure to utilize, essential nutrients does not mean that there is an overabundance of them; nor do bulging granaries and cold-storage warehouses imply that we are well fed, for it takes money (Fig. 20.2), knowledge, and vision to obtain and utilize foods wisely[36]. The following quotations, the first by a nutritional expert of the U. S. Department of Agriculture and the second by a nutritional expert of the U. S. Public Health Service and a member of the Nutrition Committee of the National Research Council, indicate the contrary.

"Millions of people in this country are living on diets that are below the safety line . . . a third or more of the families in the United States subsist on diets that should be classed as poor, . . . that take a toll in chronic fatigue, shifting aches and pains, certain kinds of digestive disturbances"[37].

"About 50 per cent of the children studied in Pennsylvania in 1939 were anemic[38]. In terms of adequate food for everyone, no food surplus has ever existed . . . the world has never had enough to eat. So-called over-production . . . is in reality failure to secure adequate distribution . . . Faulty food distribution is the most important contributory factor to malnutrition, and ignorance of the rules of good diet plus indifference to the consequences and bad dietary habits are the contributory underlying causes. Great Britain has shown that a national food policy based on nutritional adequacy can control malnutrition . . . In spite of poorer living conditions incident to war, the 1942 infant mortality in Britain was the lowest on record, and health has been maintained at a high level with a decreased general death rate and a negligible incidence of deficiency diseases . . . Such diverse problems are involved as the control of crop production, farm machinery, manpower, food distribution, transportation, food preservation and processing, storage and food preparation as well as education and diganosis, prevention, and treatment of deficiency diseases"[38].

One is tempted to quote President Roosevelt's remarks on this subject[39] ". . . every survey of nutrition shows that there is in the United States undernourishment which is widespread and serious . . . We do not lack . . . the means of producing food in abundance and variety. Our task is to translate this abundance into reality for every American family"[39].

However, our ability to serve as the "bread basket of the world" or even to produce food in "abundance and variety" is doubted by many competent agriculturists, who feel that supplying food to furnish some 4000 Calories per day for each of the 135 million persons is itself a task of gigantic proportions which, unless the soil is carefully husbanded, threatens to turn much of our own "bread basket" into a "dust bowl" by overcultivation. The report to the Food Advisory Committee, a Sub-committee on United States Food Allocation Policy, indicates that "the United States has never been and cannot become the food basket of the United Nations. U. S. food production, though impressive in itself, has never been more than a small fraction of total world production, and U. S. exports do not constitute more than a small percentage of the total food moving in world trade".

The social nutritionists ideal is an adequate diet for every member of society, at least for every child, since it is futile, for example, to furnish educational opportunities to malnourished children who, because of their malnourishment cannot utilize these opportunites efficiently; and the same holds true for other members of the community. A corollary aim should be to acquaint every consumer with the simplest and most economical menus that would furnish all the nutrients in optimal proportions. The soybean makes a good base for such a menu, and is gaining rapidly in consumer favor. The U. S. Government has called for over a billion pounds of soybean meal to be converted into flour for human consumption in 1944, much of which, however, is intended for Europe. But in this country habituated to wheat and milk, a whole wheat-whole milk bread[40] in certain proportions (6 to 20 per cent milk solids in relation to flour) when supplemented with vitamin C, is virtually a complete food. (If defatted milk solids are used, the bread would also have to be supplemented with vitamin A.) Some day, maybe those who cannot afford to buy an adequate diet, at least children, will be furnished free such a whole wheat-whole milk bread, thereby avoiding irreparable malnutrition.

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[36] Stiebeling, *et al.*, "Dietary levels", U. S. Dept. Agr. Misc. Pubs. 405 and 452, 1942. Stiebeling and Phipard, E. F., "Diets of wage earners", U. S. Dept. Agr. Circ. 507, 1939. Mack, P. B., *et al.*, "Nutrition of families on different economic levels", *Am. J. Med. Sci.*, **199**, 686 (1940); *J. Am. Diet Assn.*, **18**, (1942). Wiehl, D. G., and Kruse, H. D., *Milbank Mem. Fund. Quart.*, **19**, 241 (1941).

[37] Stiebeling, H. K., U. S. Dept. Agr. Misc. Pub. 430, 1941.

[38] Sebrell, W. H., *J. Am. Med. Assn.*, **123**, 280, 342 (1943). Lively, C. E., and Lionberger, H. F. ("Physical status of farm tenants and farm laborers in Missouri", Univ. Missouri Agr. Exp. Sta., Columbia, Mo , 1942, Prelim. Pub 1), reported substantially similar prevalence of nutritional anemia in Missouri. See also report of the committee on diagnosis and pathology, Food and Nutrition Board, National Research Council, No. 109, Nov., 1943.

[39] Proc. National Nut. Conference for Defense, Federal Security Agency, U. S. Sup. Documents, 1942.

The following are two examples of simplified menus—which do not appear to the writer as simple—for adults suggested by the National Research Council (N.R.C. circular 115, 1943).

I

1 pint milk
1 egg
1 (or more) serving of meat or fish
1 (or more) potato
2 vegetables, one green or yellow
2 fruits, one citrus or tomato
Cereal or bread, whole or "enriched"
Other foods as desired

II

1 cup turnip greens
3 sweet potatoes
20 peanuts or 3 tablespoons of peanut butter
1½ oz. beans or peas
1 cup tomatoes
3 oz. cornmeal
3–4 oz. enriched flour
⅓ quart milk
Small serving lean pork, 3–4 times per week
Molasses, fat, etc. to complete meals

Whole wheat-whole milk bread and "other foods as desired" would be a much simpler and more practical menu.

The most conspicuous constructive wartime nutritional development is dehydration and compressing of foodstuffs, which may thus be preserved for long periods and transported long distances. "The weight of bombs dropped in the Ruhr in May as given in the daily press was 8,800 tons. This weight of dried milk would yield 4,000,000 pints of liquid milk a day for 31 days, about half a pint for every head of the population in a country the size of Belgium or Portugal"[40a]. Compressed dry meat has about 30 per cent of the weight and 15 per cent of the volume of fresh meat; compressed dry egg has about 20 per cent of the weight and 10 per cent of the volume of fresh eggs; compressed dry milk has about 12.5 per cent of the weight and 10 per cent of the volume of fresh milk. The vitamin loss in milk is mostly in ascorbic acid (20 per cent loss in each drying and storage for about a year) and thiamine (about 10 per cent loss in drying and 20 per cent in storage). These developments promise to revolutionize the food-catering industry. Dry milk is already being sold (on an experimental scale) in some grocery stores (Sect. 21.2).

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[40] Taylor, A. E., *J. Am. Med. Assn.*, **81**, 892 (1923), and Stanford University Food Research Studies, **5**, No. 4 (1929). Mitchell, H. H.[38].

[40a] Barcroft, J., *Nut. Abstr. Rev.*, **13**, 1 (1943); *Nut. Rev.*, **2**, 141 (1944).

20.3. The *ad libitum* and paired-feeding methods for the nutritional evaluation of foods. The usual method for comparing the nutritional values of two rations, or some limiting nutrient (such as protein, vitamin, mineral) in the ration, is to feed them to two groups of immature test animals, for example, to litter-mate rats A and B of the same sex, weighing 50 to 80 g at the beginning of the trial. If, for example, rat A grows more rapidly than rat B, the ration fed to rat A is nutritionally superior to that fed to rat B. Here the growth rate of immature rats is taken as a measure of the nutritive values of the two rations.

This example is an obvious oversimplification. For instance, some rations not only accelerate growth but also accelerate senescence, which is not so good, and they may have unfavorable effects on other processes such as reproduction, lactation, egg production, muscular work, and so on.

Moreover, speaking from the energetic-efficiency viewpoint, two animals may gain weight at different rates, yet gain energy at the same rate. This is because some types of weight gains involve greater energy storage per unit live weight than others. For instance, one gram of protein gain is necessarily associated with three grams of water gain, whereas one gram of fat gain is not so associated with water gain. Moreover, the energy equivalent of one gram fat is 2¼ times that one gram protein. Hence, one gram fat gain is calorically equivalent to about eight grams protein gain (including the associated water). Indeed, it has been demonstrated by one group of investigators[41] that, despite differences in weight gain of rats fed the same amounts of food containing different percentages of protein, there was no difference in *energy* gain.

There is some disagreement, however, on the equality of energy gain on rats paired to the same dietary energy containing different protein percentages and inducing different growth rates[42]. For instance, the following data[42] indicate that the pair-fed rats gained different amounts of energy. The differences between Hogan's and Forbes' results may be only apparent due to methodologic differences.

The Influence of Protein Percentage in Diet on Growth Rate and Energy Storage (after Forbes, *et al.*).

Dietary protein (%)	Weight gain (12 wks) (g)	Energy stored (12 wks) (Cal.)	Nitrogen stored (12 wks) (g)	Digestibility (%)		Maintenance heat (Cal.)
				Feed energy	Feed nitrogen	
10	79	217	2.51	91.5	88.1	1709
15	107	263	3.68	91.8	91.8	1668
20	119	296	4.08	92.9	93.3	1642
25	119	302	4.17	93.4	94.2	1626

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[41] Johnson, S. R., Hogan, A. G., and Ashworth, U. S., "The utilization of energy at different levels of protein intake", Univ. Missouri Agr. Exp. Sta. Res. Bull. 246 (1936).

[42] Forbes, E. B., *et al.*, *J. Nut.*, **10**, 461 (1935); **15**, 285 (1938); **18**, 47, 157 (1939); **20**, 47 (1940); *Science*, **99**, 476 (1944). Hamilton, T. S., *Id.*, **17**, 583 (1939); **18**, 565 (1939); Brody, S., *Ann. Rev. Bioc.*, **4**, 399 (1935).

Most important from the present viewpoint is that the ration offered to (the more rapidly growing) rat A may be more palatable or otherwise stimulate a higher food consumption, so that the higher growth rate of rat A may be due not to the superiority of its limiting nutrient as such but to the fact that it stimulates a greater food consumption.

One could, of course, partly overcome this confusing situation by expressing the growth rate in terms of weight gains per unit food consumed, such as by the efficiency equation we used (Ch. 1):

$$\text{Growth efficiency} = \frac{\text{weight gain (energy units)}}{\text{feed consumed (energy units)}} \qquad (20.1)$$

Osborne and Mendel[43] defined the nutritive value of protein by a similar equation:

$$\text{Nutritive value of protein} = \frac{\text{weight gained}}{\text{protein consumed}} \qquad (20.2)$$

and McCollum and associates[44] defined it by the relation:

$$\text{Nutritive value of protein} = \frac{\text{nitrogen retained in body}}{\text{nitrogen consumed}} \qquad (20.3)$$

The objection to the above method for compensating for differences in food intake is that the animals consuming more food grow larger and have a correspondingly higher maintenance cost. Theoretically, the situation is confused by the maintenance factor.

Osborne and Mendel[45], therefore, suggested what is now called the "paired-feeding method" involving equalization in food intake in test animals. As indicated by the following table[45], the idea is to have the animals on the various diets under investigation consume equal amounts of food (438 g) in the same time (77 days). The relative weight gains are supposed to indicate the relative qualities of the protein under investigation. Thus in the following table, the rats are seen to gain 71 grams on the ration containing 8 per cent casein, 77 grams on the one containing 8 per cent lactalbumin, and so on.

Osborne and Mendel also used a combination of food equalization and body-weight equalization methods for comparing the growth-promoting properties of different proteins; they adjusted the various protein percentages so that all the assay animals made equal weight gains. The ideal condition for comparing biologic values was considered to be attained when animals of similar weight and age "eat the same amount of food in the same number of days and gain the same amount of weight, the protein factor being the only variable".

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[43] Osborne, T. B., Mendel, L. B., and Ferry, E. L., "A method of expressing numerically the growth-promoting value of proteins", *J. Biol. Chem.*, 37, 223 (1919). See also Osborne and Mendel, "The comparative nutritive value of certain proteins in growth, and the problem of the protein minimum", *J. Biol. Chem.*, **20**, 351 (1915). (Here weight gains were related to protein intake when the ratio weight gain per protein consumed is maximum The different proteins were fed at 9 to 10 per cent levels for 9 weeks. The animals were fed *ad libitum* because of the belief that the rats consume food in proportion to caloric rather than protein needs.)

[44] McCollum, E. V., Orent-Keiles, E., and Day, H. G., "The newer knowledge of nutrition", Macmillan, pp. 126–27, 1939.

[45] Osborne, T. B., and Mendel, L. B., "A quantitative comparison of casein, lactalbumin, and edestin for growth or maintenance", *J. Biol. Chem.*, **26**, 1 (1916). This method was also used by Hopkins, F. G., *J. Physiol.*, **44**, 425 (1912).

Relative Weight Gains of "Pair-fed" Rats in Relation to the Level and Nature of Dietary Proteins.

Protein	Protein in diet (%)	Food intake (g)	Length of trial (days)	Weight gain (g)
Lactalbumin	14.8	438	77	22
Lactalbumin	8.0	438	77	77
Edestin	8.0	438	77	50
Casein	8.0	438	77	71
Casein plus cystine	8.0	438	77	95
Casein	10.8	438	77	85
Casein	16.2	438	77	105

A great deal has been written for and against the "paired-feeding"[46] and "body-weight equalization"[47] methods for evaluating foods.

The distinctive feature of the paired-feeding method is that the food-energy intake of the assay animals on all rations is equalized to the level of the animal consuming the least food.

The advantage of the body-weight equalization method is that the maintenance cost is more likely to be the same for the animals on the diets under comparison, and the efficiency of the productive processes is not complicated by maintenance differences. Kleiber[47] compared the nutritive effects of the same basal ration differing only in the calcium percentage, one having 10 mg and the other 430 mg calcium per 100 grams food. The rats on the low-calcium diet had poor appetites, gained slowly; the rats on the high-calcium diet were restricted in feed consumption so that they gained at the same rate as those on the low-calcium diet. To reach body weight 146 grams (at 105 days), the low-calcium rats consumed 456 grams in contrast to 372 grams consumed by the high-calcium rats. The efficiency of dietary energy utilization (as measured by weight gains at the given dietary level) is thus 1.23 times as great on the high- as on the low-calcium level. This difference in feed utilization is attributed by Kleiber to (1) higher maintenance cost on the low-calcium diet (the basal metabolism at equivalent body weight for the low-calcium rats was 1.2 to 1.3 times that of the high-calcium rats); (2) higher calorigenic effect of the low-calcium diet; and (3) greater loss of unoxidized material in feces and urine on the low-calcium diet.

Which, then, of the above two major methods, *ad libitum* or *paired feeding*, should be used in the practical nutritional evaluation of foods or feeds?

There is, of course, no difference between the two if both rations are equally palatable and are consumed spontaneously in equal amounts.

[46] See, among his other papers, Mitchell, H. H., "Some essentials of a good nutrition experiment", *J. Nut.*, **2**, 225 (1930), and **4**, 525 (1931); *Science*, **66**, 596 (1927); *J. Animal Sci.*, **2**, 263 (1943).

[47] Mitchell, H. H., and Hamilton, T. S., *Proc. Am. Soc. Ani. Prod.*, p. 241, 1935. Kleiber, M., *et al.*, *J. Nut.*, **19**, 517 (1940).

The *ad libitum* method is the obviously correct one to use if it is desired to measure the relative appetite-stimulating properties of rations and, as explained in the preceding section, appetite for natural foods is normally a very important homeostatic factor. An appetite for, or good palatability of, a food normally indicates that it is a good food. Conversely, an appetite-depressing food is normally a poor food. Thus a food lacking in thiamine or calcium leads to loss of appetite, and the animal is much better off if it does not eat that food. Equalizing the food intake would, in this case, defeat the purpose for which the experiment is conducted, namely to discover which is nutritionally the better food. Normally, the greater the food consumption the greater the speed and economy of the productive process (growth, milk production, egg production, and so on) because of the reduced overhead maintenance cost per unit food consumed. Quoting Osborne and Mendel[48], "Economy of food can be effected only by supplying the young animal with as much as it will eat. . . . The practical feeder does not wish to know what quantity of a given protein is the smallest which he can use to secure a given amount of gain . . . rather . . . the greatest gain in the shortest time".

There are many experimental procedures, however, in which the paired-feeding method is superior, if not indeed the only useful one. For instance, if it is desired to evaluate the relative nutritional availability of calcium in the same milk before and after pasteurization[49], the differences in nutritional availability would easily be wiped out by slight differences in milk intake. Where the milk intake must be strictly equalized, the paired-feeding method is the only reasonable one to use. The results can then be presented quantitatively in a table or graph in which the availabilities of the raw and pasteurized milk are plotted against dietary levels. The criterion of calcium availability should, of course, be calcium storage, not weight gain or energy gain, unless it is also desired to investigate the influence of pasteurization of milk (not merely calcium) on weight gain or energy gain. The paired-feeding method should also be used for investigating the relative availability of, for example, butterfat and vegetable fat[50], in which case the criterion of availability may be weight gain or preferably energy gain.

Summarizing, two methods are employed for comparing the nutritional values of foods: (1) *paired-feeding*, or food-equalizing, which compares the nutritional effects at an arbitrary low level set by the animal which consumes the least food; and (2) *ad libitum* feeding which permits each animal to choose its own food-intake level.

The outstanding advantage of the paired-feeding method is that it eliminates the confusion in results due to differences in food intake which may mask the effects of differences in food composition. The disadvantages of the paired-feeding method are: (1) since the food intake is equalized, the effects of the differences in the food composition are not striking; (2) the differences in nutritional effects are obtained for one feeding plane, usually a low one (set by the less appetizing food) and, therefore, not the best plane for agriculturally productive purposes requiring the greatest food intake; (3) it does not indicate palatability differences in the food; (4) the animal on the better ration whose food intake is limited, is hungrier than its pair-fed mate, and one may question whether animals differing in this respect are comparable[51]; (5) this method is not suitable for long-time investigation, including fertility and longevity.

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[48] Osborne, Mendel, and Ferry[42].

[49] Ellis, M., and Mitchell, H. H., *Am. J. Physiol.*, **104**, 1 (1933).

[50] Deuel, H. J., Jr., *Science*, **98**, 139 (1943).

The outstanding advantage of the *ad libitum* feeding method is that it places a premium on palatability, on food intake [often the best measure of nutritional quality of a feed or food, especially if the results are expressed in terms of efficiency (eq. 20.1)], or of its reciprocal, pounds feed consumed per pound live weight gained. From the agricultural viewpoint, the best ration is defined by the highest yield unit per feed consumed, regardless of feed consumption level (Fig. 20.3). Since the highest yield is usually associated with the highest food consumption level, the *ad libitum* method seems to be the more useful for practical comparisons of feed values.

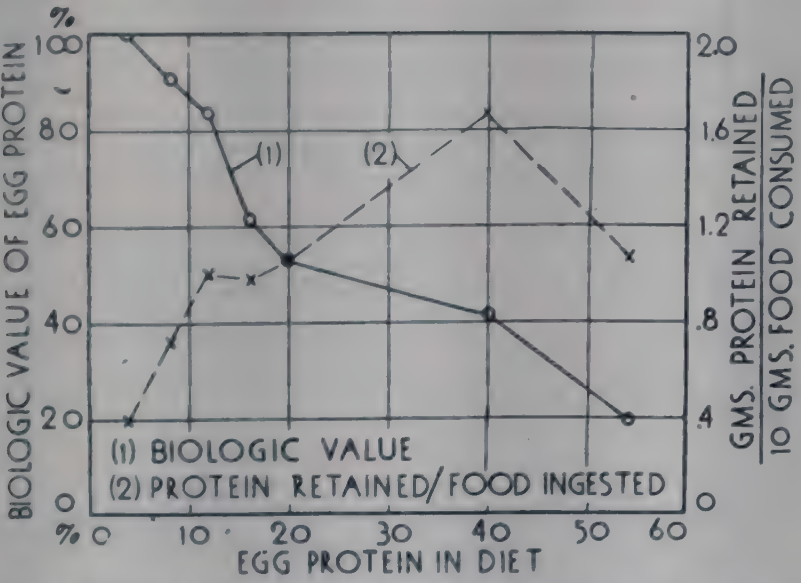

Fig. 20.3. Curve (1) shows that the apparent biological value of protein declines with increasing protein percentage in the diet; curve (2) shows that the ratio of protein retained to feed ingested increases with increasing protein percentage in the diet up to about 40 per cent, in spite of the decline in biological value. This chart was prepared by the writer from data by T. S. Hamilton as quoted by H. H. Mitchell in 1937.

Sherman and Campbell[52] employ the *ad libitum* feeding method, interpreting the results by "the application of common sense" and the use of statistical methods (standard deviation, probable error, and coefficient of variation of the means). Growth criteria for rats include the rate of growth of the young during the first 28 days after weaning, gain in weight per 100 Calories of food consumed, gain per gram of protein consumed, Calories of food per gram of body weight per day, and average weights on the different diets at all ages.

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[51] Boas-Fixsen, M. A., *Nut. Abstr. Rev.*, **4**, 450 (1934–35). Boas-Fixsen, *et al.*, *Bioc. J.*, **28**, 592 (1934).

[52] Campbell, H. L., "Growth, reproduction and longevity as research criteria in the chemistry of nutrition", Dissertation, Columbia University, 1928. Sherman, H. C., and Campbell, *J. Biol. Chem.*, **97**, p. iii (1932); *Proc. Nat. Acad. Sci.*, **20**,413 (1934).

The reproduction criteria include ability to bear and rear young, average weight of young at weaning time, length of breeding period, and age of sexual maturity. Longevity records are kept.

McCollum's method[53] for the long-range effects of proteins consisted in feeding diets containing the same percentages of the proteins under comparison, and observing the performance (growth rate, fertility, and lactation for 2 generations). McCollum kept no record of feed intake assuming that rats consume food in proportion to their caloric (not protein) needs. Nor did McCollum make adjustment for maintenance or digestion expenses.

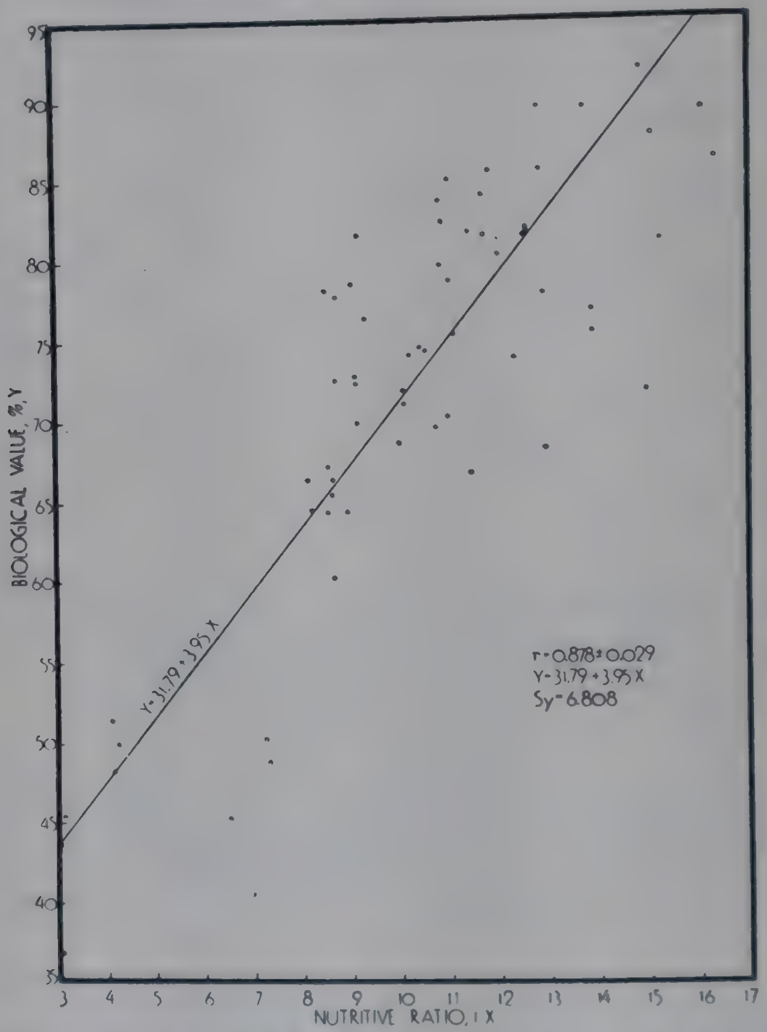

Fig. 20.4a. Indicates that the higher the protein percentage in the ration (that is, the lower the nutritive ratio, which is the ratio of the digestible protein calories to the digestible non-nitrogenous calories) the lower the apparent "biological value" of the protein (p. 778).

20.4. Balance between nutrients. The above discussions on "nutritional wisdom" and "paired-feeding" methods indicate the dependence of nutritional welfare on a certain balance between the consumed nutrients.

The mechanisms whereby certain dietary interrelations affect health are known or suspected in some cases. It is known, for example (Ch. 6), that a certain amount of thiamine is necessary to oxidize in the body a given amount of carbohydrate. It is likewise clear that (when the protein in the diet is low) the proportion between the various dietary amino acids must approximate those in the body tissues, milk, egg, and so on, produced by the animal. It is also clear, for example, that there is some one proportion or balance between the (undigestible) roughage and the (digestible) concentrates in the ration which is optimal for the animal or for the productive process, such as milk production[54]. Some roughage is needed to stimulate peristalsis; too much roughage may take up space needed for digestible foods, and stimulate excessive peristalsis, thereby disturbing the normal time relations in the digestive sequence. Or it may adsorb and sweep out digestive juices, enzymes, and digestible and even digested food. A dramatic illustration of balance between vitamins previously cited (Ch. 6) is the interrelation between biotin and avidin.

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[53] McCollum, E. V., *et al.*, *J. Biol. Chem.*, 47, 111, 139, 175, 207, 235 (1921).

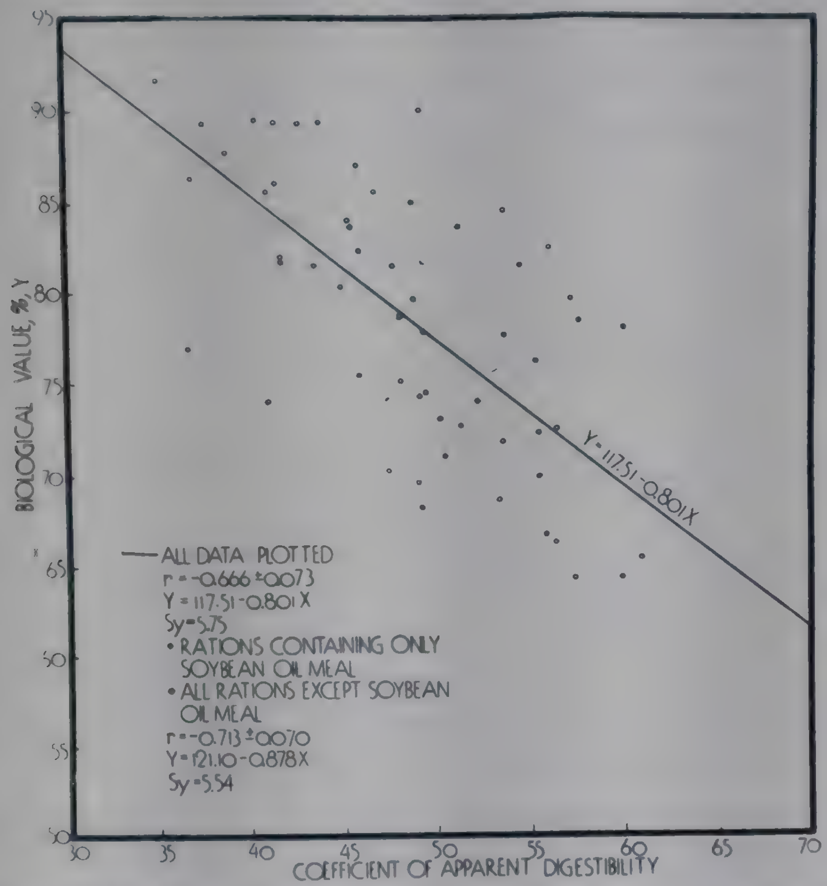

Fig. 20.4b. Indicates that the higher the apparent digestibility of a feed, the lower the apparent biological value of its protein. In other words, the apparent biological value of a protein varies inversely with its intake level (Ch. 4). There is no one definite biological value for a given protein. Figs. 20.4a and b, representing data on Holstein heifers, are from Swanson, E. W., and Herman, H. A., Univ. Missouri Agr. Exp. Sta. Res. Bull., 372, 1943 (see also pp. 757 and 778.)

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[54] Moore, L. A., and Huffman, C. F., "Bulk as a factor in formulating grain mixtures for dairy cattle", *J. Agr. Res.*, **44**, 789 (1932). Cole, H. H., and Mead, S. W., *Science*, **98**, 543 (1943).

Many types of necessary balance between foods or nutrients are not understood. For instance, dogs digest raw starch and raw egg when fed together, but cannot digest raw starch or raw egg when each is fed alone[55]. Many other examples have been cited in the preceding section, such as that of Kleiber, who reported declining food utilization on declining calcium content in the ration, and that of Forbes, who reported declining food utilization on declining protein content in the ration. Similar declines in food utilization were reported on reducing phosphate[56] and other inorganic constituents[57]. Mitchell[58] reported 40 to 50 per cent greater weight gains in chickens by adding one per cent common salt to a chick mash made up of 87 per cent corn, 10 per cent casein, 2 per cent cod-liver oil, and one per cent $CaCO_3$.

The following discussion relates to the mutually supplementary values of, or the balance between, proteins containing different available amino acids. The discussion is necessarily confined to non-ruminants since, as above explained, they are not dependent on fine balance between the dietary amino acids.

If two or more proteins possess the same limiting amino acids, they will not supplement one another. For instance, wheat, linseed, and cottonseed meals do not supplement one another because they are all deficient in the same essential amino acids, *i.e.*, lysine and tryptophane. This explains the dramatic growth-accelerating effect of adding lysine and tryptophane to such rations (Fig. 20.5). On the other hand, milk and meat proteins (rich in lysine) and seed proteins (poor in lysine) do supplement each other. "Beef protein with a biological value of 69 and flour protein with a biological value of 55 when combined in proportion of 1 to 2 have a biological value of 73"[59]. Likewise, while each alone, corn or tankage, is of low nutritive value, the two in combination make a satisfactory feed for swine[60]. The extremely high supplementary value of milk to cereals is discussed in detail elsewhere[61] (Sects. 20.2 and 21.2).

Heating often changes the biological value of proteins. For example, heating milk tends to reduce the biological value of its protein[62] because milk contains lysine and cystine which are sensitive to heat. Beef-muscle proteins likewise suffer a reduction (about 10 per cent) in biological value on

[55] Childrey, J. H., Alvarez, W. C., and Mann, F. C., "Digestion efficiency with various foods and under various conditions", *Arch. Inter. Med.*, **46**, 361 (1930).

[56] Kleiber, M., Goss, H., and Guilbert, H. R., *J. Nut.*, **16**, 392 (1936). Riddell, W. H., *et al.*, Kansas Agr. Exp. Sta. Res. Bull. 36, 1934. Aubel, C. E., *et al.*, *Id.*, Tech. Bull. 41, 1936. Eckles, C. H., and Gullickson, T. W., Minn. Agr. Exp. Sta. Bull. 91, 1932. Morris, S., *Bioc. J.*, **33**, 1209 (1939).

[57] Kriss, M., *J. Nut.*, **16**, 385 (1938). Kriss and Smith, A. H., *Id.*, **14**, 487 (1937).

[58] Mitchell, H. H., and Carman, G. G., *J. Biol. Chem.*, **68**, 165 (1926).

[59] Mitchell, H. H., and Smuts, D. B., *J. Biol. Chem.*, **95**, 263 (1932).

[60] Mitchell and Kick, C. H., *J. Agr. Res.*, **35**, 857 (1927).

[61] See Hart, E. B., and Steenbock, H., *J. Biol. Chem.*, **38**, 267 (1919), for an early study of the relative supplementary values of milk, tankage, and alfalfa proteins.

[62] Fairbanks, B. W., and Mitchell, H. H., *J. Agr. Res.*, **51**, 1107 (1935). Henry, K. M., *et al.*, "The effect of pasteurization on biological value and digestibility of its protein", Nat. Inst. Res. in Dairying, Reading, Eng., 1937.

boiling[63]. The biological value of beans—especially soybeans—is, on the contrary, greatly increased by heating[64]. The biological values of fish[65] and nut proteins are apparently unaffected by heating.

There is nothing novel about the idea that a diet or a ration needs to be well balanced for the needs of a particular process and that the waste of nutrients is least and the efficiency highest when the ration is most perfectly balanced. The novel aspect is the understanding of the mechanisms involved in terms of food composition and oxidation mechanisms (Ch. 6), especially in relation to the specific dynamic effect of foods (Sect. 2.3 and Ch. 4), and the relation between such avoidable wastes and thermodynamically unavoidable expenses (Ch. 2) in the efficiency complex.

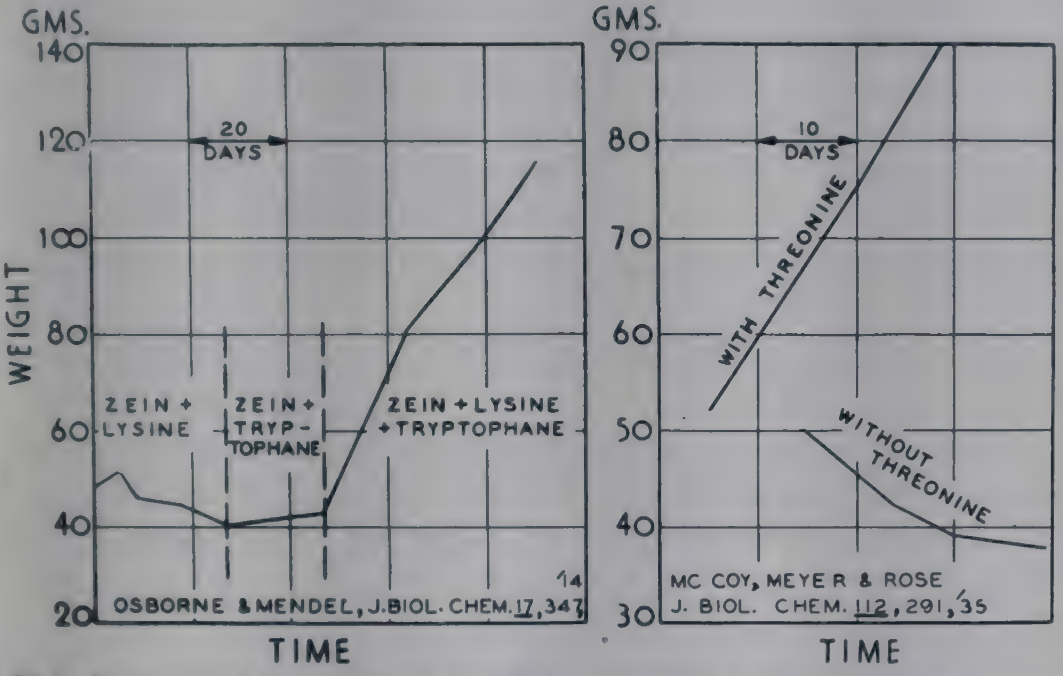

Fig. 20.5. Lysine and tryptophane are dietary-essential amino acids as demonstrated by the curve showing cessation of growth when rats are fed on a diet in which zein (which lacks lysine and tryptophane) is the sole protein, and good growth when this diet is supplemented by lysine and tryptophane. The curves on the right show similarly that threonine is a dietary essential not only for growth but, judging by weight loss, also for maintenance.

Some of these ideas have been attractively, often dramatically, generalized such as Mitchell's: "Probably . . . unbalanced rations, like toxic substances, exert harmful effects in proportion to the amounts consumed . . ."[66] and "Each improvement in the nutritive balance of a ration improves the efficiency of its utilization. . . . It is a rational deduction from Liebig's 'law of the minimum' that a deficiency of a ration in an indispensable nutrient will impair the utilization of all other nutrients and hence the net energy of the ration"[67]; or Forbes'[68] formulation of a "law of maximum normal nutritive value", to the effect that a perfectly balanced ration is one in which there are "no nutritive deficiencies to compromise the significance of the net energy value".

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[63] Morgan, A. F., *J. Nut.*, 7, 367 (1934). See also *J. Biol. Chem.*, **90**, 771 (1931) (heat on casein and cereals.)

[64] Waterman, H. C., and Johns, C. O., *J. Biol. Chem.*, **46**, 9; **47**, 285 (1921). Hayward, J. W., *et al.*, *J. Nut.*, **11**, 219 (1936). Wilgus, H. S., Jr., *et al.*, *Ind. Eng. Chem.*, **28**, 586 (1936).

[65] Maynard, L. A., *Ind. Eng. Chem.*, **24**, 1168 (1932). Schneider, B. H., *J. Agr. Res.*, **44**, 723 (1932). Wilder, O. H. M., *et al.*, *Id.*, **49**, 723 (1934).

[66] Mitchell, H. H., *Science*, **80**, 558 (1934).

These generalizations about balance between nutrients must not be taken in too narrow a sense. A ration is balanced not at a sharply defined point but in a rather wide zone with considerable freedom of change in proportions between the nutrients. This elasticity of balance between nutrients is of great practical importance because it permits taking advantage of variability of supply and price of various dietary components.

The above generalization on dietary balance, moreover, needs broadening to include the time element, involving long-range effects, perhaps over several generations. For instance, it appears that very rapid growth in dairy calves induced by dietary means often leads in later life to particularly poor lactational performance. The same may be true as regards longevity, which may be depressed by rapid growth (Sect. 18.2.4). The method of assay by growth rate of rats is, perhaps, being over-emphasized. It was previously noted that some investigators judge the values of rations not only by growth rate but also by their effects on the whole life histories of the animals. This long-range method of dietary assay needs to be further extended.

20.5. General vitamin relations in nutrition. Chapter 6 was concerned with vitamins in relation to enzyme action in oxido-reduction processes. We shall here discuss the better-known aspects of vitamins in the nutrition of different species (Fig. 20.6).

It may be useful to recall that 15 vitamins have been isolated, namely, A, D, E, K, B_1 (thiamine), B_2 or G (riboflavin), B_6 (pyridoxine), C (ascorbic acid), niacin (nicotinic acid), pantothenic acid ("filtrate factor"), biotin, inositol, *p*-aminobenzoic acid, choline, and B_c (chick antianemic factor, obtained from the norite eluate fraction of liver extract, probably identical with or a component of "folic acid", an essential growth-accelerating factor for *Lactobacillus caseii*). There are several other vitamins which are not well known, such as vitamin P or citrin, vitamins[68a] B_{10} and B_{11}, and so on.

Not all these vitamins are needed in the diet of all species of higher animals. For instance, as previously explained, ruminants are not dependent on their feed for the water-soluble vitamins. Indeed, if they have access to bright sunshine, ruminants are dependent on their feed for only one vitamin, A, or rather for the provitamin A, carotene (plants have no vitamin A), and the demand for this vitamin in ruminants is very large, perhaps ten-fold the theoretical minimal need[69] because much of it is destroyed in the rumen.

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[67] Mitchell, H. H., "Conference on energy metabolism", National Research Council, 1935, p. 83.

[68] Forbes, E. B., *Science*, **77**, 306 (1933). See also Forbes, ref. **42** (1944).

[68a] Elvehjem, *et al.*, *Proc. Am. Chem. Soc.*, p. 15B (1944).

[69] Hart, G. H., *Nut. Abstr. Rev.*, **10**, 261 (1940).

Then, too, different species utilize carotene with different efficiencies. Poultry utilize it much more efficiently than cattle or even swine. Man can utilize about 60 per cent of dietary carotene, that is, the vitamin A equivalent of carotene for man is only a little over half that of fish oil vitamin A[70].

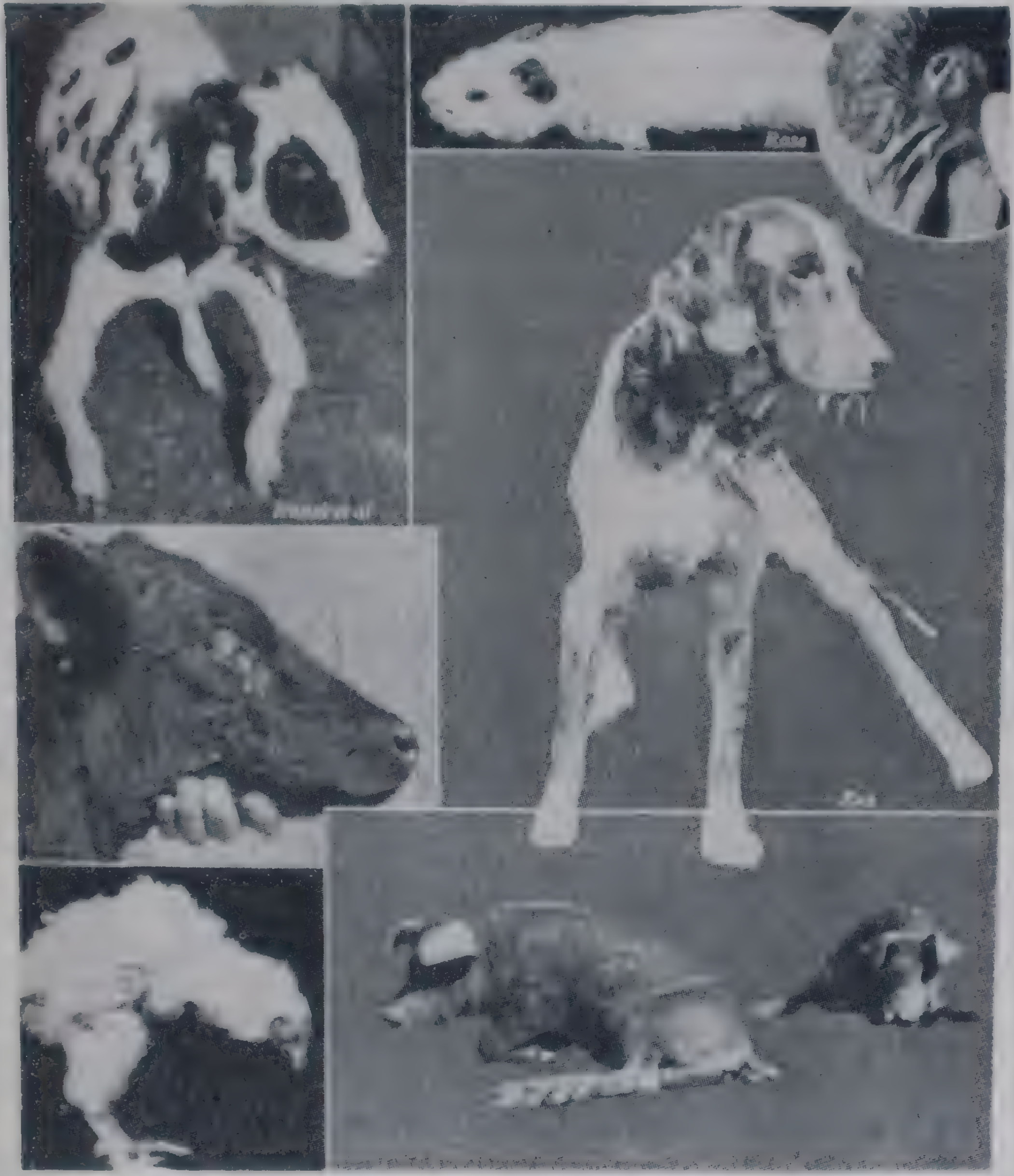

Fig. 20.6. Typical appearance of animals suffering from vitamin deficiency: deficiency of vitamin D in a calf (upper left), vitamin A in a calf (middle left), vitamin B_1 in a chick (lower left), scurvy in a guinea pig, nicotinic acid in a dog, vitamin A in swine, vitamin A in a chicken (upper right). From R. Graham and H. H. Mitchell, Circular 449, Univ. Ill. Agr. Exp. Sta.

The storage capacity for vitamins also differs. Vitamin A is rapidly stored in large amounts and used as needed[71]. Vitamin A appears to be needed by all species of mammals and birds.

Dietary ascorbic acid (and citrin?), on the other hand, is apparently needed by anthropoids and guinea pigs only.

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[70] Booher, L. E., *et al.*, *J. Nut.*, **17**, 317 (1939).

[71] Guilbert, H. R., and Hart, G. H., *J. Nut.*, **8**, 25 (1934).

Dietary nicotinic acid is not needed by the rat, mouse, and chick, but it is apparently needed by the other species investigated (except, of course, ruminants).

Dietary thiamine, riboflavin, pyridoxine, and pantothenic acid are apparently needed by all species investigated (except ruminants), but variable amounts of these vitamins are also produced by microorganism in the digestive tracts of all species, even in man[72].

Dietary vitamin E does not appear to be needed by goats and swine[72a], but it is definitely needed by the rat, mouse, hamster, guinea pig, rabbit, chick, turkey, dog, and duck.

p-Aminobenzoic acid is apparently produced by microorganisms in the digestive tract in sufficient amounts to meet all needs. This is indicated by the fact that feeding sulfa drugs (which inhibit these microorganisms from producing PAB, see Sect. 7.1) leads to deficiency symptoms, cured by administering of PAB[72b]. Normally, biotin and vitamin K are apparently also produced by intestinal bacteria in sufficient amounts to meet all human adult needs. If, however, sulfanilimides are included, dietary vitamin K is needed by the rat, mouse, guinea pig, rabbit, pigeon, chicken, duck, goose, and canary, and dietary biotin is needed by chickens and turkeys.

Dietary choline is needed by the rat, rabbit, chicken, turkey, and dog.

Dietary inositol is needed by the mouse and chick.

The nature of the diet tends to influence the vitamin need, not only because of its effect on the vitamin-producing activity of intestinal microorganisms but also because thiamine, for example, is more involved in carbohydrate-rich[73] than in fat-rich or protein-rich[74] diets.

Some processes, especially reproductive, such as gestation, lactation, production of fertile eggs, appear to need extra vitamin supply.

Age influences the amount of dietary vitamin need. Old age is usually associated with decreased utilization and, therefore, with need for larger intake of vitamins[75]. Youth and rapid growth also call for increased vitamins, but for different reasons. Heuser[76] believes that the riboflavin need in chicks is not proportional to the feed consumption or to the body weight of young animals but to the relative growth rate; during the first week of growth chicks require over threefold riboflavin per unit food consumed than during the eighth week.

The need for pantothenic acid is particularly high in early life when growth is most rapid. Thus rats seem to need four times the pantothenic acid at

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[72] Najjar, V. A., and Holt, L. E., Jr., "Biosynthesis of thiamine in man", *J. Am. Med. Assn.*, **123**, 683 (1943). Holt and Najjar, *Lancet*, **63**, 366 (1943).

[72a] McRoberts and Hogan, *J. Nut.*, **28**, 165 (1944).

[72b] Elvehjem, C. A., *Am. Scientist*, **32**, 35 (1944).

[73] Arnold, A., and Elvehjem, C. A., *Am. J. Physiol.*, **126**, 289 (1939).

[74] Wainio, W. W., *J. Nut.*, **24**, 317 (1942).

[75] Irving, J. T., and Richards, M. B., *Nature*, **144**, 908 (1939).

[76] Heuser, G. F., *et al.*, *Poultry Sci.*, **17**, 105 (1938).

3 weeks than at 10 weeks[77]. Smaller-younger (growing) animals need more pantothenic acid per unit body weight than the heavier-older[78] animals.

As most vitamin investigations involving the use of highly purified diets have been conducted on rats, the dietary requirements of this species are best known. Several investigators, indeed, succeeded in growing rats on synthetic diets composed of dextrose, casein, hydrogenated oil or corn oil, and salt mixture supplemented with 8 vitamins: A, D, E, thiamine, riboflavin, pyridoxine, calcium pantothenate, and choline[79]. The males were apparently fertile, but not the females. One group of investigators reported[80] that young could not be obtained on this diet even if supplemented with nicotinic acid because "in each case the female apparently destroyed the male".

More recent reports indicate rearing of rats through 3 to 4 generations on diets composed of dextrose, casein, hydrogenated oil, salts, cod-liver oil, supplemented with 6 other vitamins: thiamine, riboflavin, pyridoxine, nicotinamide, pantothenic acid, and choline[81]; or on diets composed of sucrose, casein, salts, corn oil, halibut-liver oil, supplemented with thiamine, riboflavin, pyridoxine, nicotinic acid, pantothenic acid, choline, and α-tocopherol[82]. The rearing is apparently associated with lactation difficulties.

Normal growth and fair reproduction in rats were observed by the Missouri investigators[83] on synthetic diets supplemented with 12 vitamins: A, D, E, K, thiamine, riboflavin, pyridoxine, pantothenic acid, nicotinic acid, choline, inositol and *p*-aminobenzoic acid. Some factors present in beef-liver extract and absorbed therefrom on fuller's earth increase the weaning percentage to 90 per cent and better, apparently by its favorable effect on the composition of the milk, because without it the young rats die, although the stomach is filled with milk. Yeast does not furnish the missing factor to rats[84] or rabbits[85]. In some cases the difficulty may be quantitative; there may not be enough of certain vitamins in the diet. Lactation makes especially large demands on *p*-aminobenzoic acid, thiamine, and riboflavin[86]. Such difficulties would not occur in ruminants that produce their own B vitamins.

The question of whether or not a given diet is adequate depends on the physiologic age and length of the experimental period. A given diet may be adequate for a short period at a given age but not for a longer period, or for another age interval. The following nitrogen-free dietary base has been recently used[87] for 4-week feeding periods in rats.

Thiamine hydrochloride	224	mcg	Choline chloride	134	mg
Riboflavin	400	mcg	*p*-Aminobenzoic acid	1.0	mg
Pyridoxine hydrochloride	243	mcg	Cod-liver oil	2	g
Calcium pantothenate	1.5	mg	Corn oil	10	g
Nicotinic acid	2.5	mg	Salt mixture	4	g
Starch and amino acids to make	100	g			

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[77] Unna, K., and Richards, G. V., *J. Nut.*, **23**, 45 (1942).

[78] Schaefer, A. E., *et al.*, *J. Biol. Chem.*, **143**, 321 (1942).

[79] Richardson, L. R., Hogan, A. G., Long, B., and Itschner, K. F., *Proc. Soc. Exp. Biol. Med.*, **46**, 530 (1941).

[80] Frost, D. V., *et al.*, *Id.*, **46**, 407 (1941).

[81] Unna, K., *et al.*, *J. Nut.*, **22**, 553 (1941).

[82] Henderson, L. M., *et al.*, *Id.*, **23**, 47 (1942).

[83] Richardson, Long, and Hogan, *Proc. Div. Biol. Chem., Am. Chem. Soc.*, p. 4, 1942.

[84] Ball, Z. B., and Barnes, R. H., *Proc. Soc. Exp. Biol. Med.*, **48**, 692 (1941).

[85] Hogan, A. G., and Hamilton, J. W., *J. Nut.*, **23**, 533 (1942).

[86] Sure, B., Univ. Ark. Agr. Exp. Sta. Bull. 252, 1930. and 425, 1942; *J. Nut.*, **19**, 57 (1940); **22**, 499 (1941); **26**, 275 (1943).

[87] Albanese, A. H., and Irby, V., *Science*, **98**, 286 (1943). Kinsey, V. E., and Grant, W. M., *Id.*, **99**, 303 (1944).

The optimal vitamin *proportions* in human nutrition are usually said to be 1 mg thiamine: 2 mg riboflavin: 10 mg nicotinic acid: 30 mg ascorbic acid: 4000 I. U. vitamin A: 400 I. U. vitamin D.

The quantitative aspects of vitamin need—the amounts required in relation to body size and to food consumption—have been discussed in Chapter 15. The conclusion there reached was that the B vitamins, which function as general metabolic catalysts, are needed in direct proportion to the total energy metabolism, or in direct proportion to the total caloric food intake. Thus the minimal thiamine need appears to be about 1 mcg thiamine per gram dry food consumed, or about 300 mcg per 1000 Calories energy metabolism. The optimal thiamine need is, perhaps, 500 to 1000 mcg (0.5 to 1.0 mg) per 1000 Calories metabolism. The minimum riboflavin need per food Calorie appears to be about twice the minimum thiamine need.

The need for the specialized fat-soluble vitamins, and particularly for vitamin A, seems to be in proportion to simple body weight rather than to energy metabolism. The minimal vitamin A need appears to be 2 to 4 mcg per pound live weight, regardless of species.

Because of the large literature on the quantitative vitamin needs of different animals, the quantitative data together with the references are presented in the following tables prepared with the cooperation of Dr. V. F. McRoberts.

Special attention is called to the wide range of data by Guilbert and associates and the remarkable consistency of the ratio of vitamin A to unit body weight in animals of such wide range in live weight. The vitamin A need for poultry (data not by Guilbert) appears to be much higher than for mammals.

In this connection it may be helpful to have recorded the quantitative vitamin unit equivalents. Vitamin A is usually represented in I. U. (International Units) or U. S. P. units (identical with I. U. for vitamin A); thiamine and riboflavin in mg or in mcg (micrograms or gamma, which is 1/1000 mg or 1/1,000,000 g); ascorbic acid and nicotinic acid in mg. The equivalents are:

1 I. U. vitamin A = 1 U. S. P. unit = 0.6 mcg B-carotene. (The Sherman-Munsell unit of vitamin A, about 1.4 I. U. vitamin A, is defined by the amount needed to support growth in a "standard rat" for 8 weeks at the rate of 3 g per week.)
1 mg thiamine = 333 I. U.
1 I. U. thiamine = 3 mcg thiamine hydrochloride
2½ mg riboflavin = 1000 I. U.
(1 Sherman-Bourquin unit riboflavin = 2.5 mcg or
1 mcg = 0.4 Sherman-Bourquin unit)
1 mg l-ascorbic acid = 20 I. U.
1 Sherman unit ascorbic acid = 10 to 15 I. U.
1 I. U. vitamin D = 0.025 mcg crystalline vitamin D, or
1 mcg vitamin D (calciferol) = 40 I. U.
1 Steenbock unit vitamin D = 3.3 I. U.

The vitamin content of food is often expressed in terms of micrograms per 100 gm of the food. It is useful to remember that 100 g is 3½ oz, the usual weight of a serving (3½ oz = 99.2 g; 4 oz = 113.4 g).

The minimal vitamin need is estimated[88] by the minimal intake which permits normal growth and development in the young of a given age; or in adults the minimal intake which prevents development of typical lesions and/or loss in weight. The minimal amount of the vitamin required to cure deficiency symptoms is also used. The latter method gives higher values and some of the published differences in vitamin need are due to these differences in method employed. Vitamin A deficiency in man by the dark-adaptation method as used by Booher is more sensitive than the night-blindness test used by Guilbert, with corresponding apparently higher vitamin A needs in man than in farm animals.

The estimation of the amounts of vitamin in food[88] is done in several ways, including chemical determination, growth rate of an appropriate assay animal, and for the members of the B complex vitamins, by microbiologic methods.

Since yeast, molds, bacteria are specific in their nutritive requirements, the growth rate of the microorganism under controlled conditions is directly proportional to the vitamin concentration in the test substance. Various strains of yeast (*Saccharomyces cerevisiae*) are used for estimating[89] thiamine, pyridoxine, biotin, inositol. Growth rate is measured by the rise in medium turbidity or CO_2 accumulation. Pyridoxine may also be measured[90] by weighing the mycelium of the mold *Neurospora sitophila*. *Lactobacillus caseii* is employed[91] for estimating riboflavin, biotin, and pantothenic acid. The measurement consists in titrating the lactic acid produced during a given growth period. *Lactobacillus arabinosus* is employed[92] for estimating niacin.

Ascorbic acid is usually estimated by the chemical method of Bessey and King[93]. The food sample is extracted and the extracted ascorbic acid is titrated with 2,6-dichlorphenolindophenol, a deep purple dye in neutral solution. The dye is reduced by the ascorbic acid to a colorless form. The quantity of dye reduced is a measure of the ascorbic acid. Certain types of materials, however, yield misleading results, in which case the Sherman guinea pig method is used[94].

Depending on the nature of the material tested, vitamin A may be estimated (for fish oils) spectrophotometrically or colorimetrically through its reaction with antimony chloride or (for plant material) extracting the carotene pigments and estimating, or by the growth method[95].

Vitamin D is estimated by confining young rats for 3 weeks to a ricket producing diet, followed by 8-day feeding of the test material. On the eleventh day the animal is sacrificed and the tibia, or radius, or ulna dissected out, cleaned, finally immersed in silver nitrate solution and exposed to light. Silver is deposited where calcium is present in the metaphysis of the bone forming a dark line, indicating the extent of calcium deposition, and the degree of healing due to feeding the test food. This is the "line test"[95] for vitamin D. Other methods are also used, such as roentgenological examination of the animal or determination of the bone ash.

Vitamin K is estimated by the blood clotting time[96].

[88] For a recent extensive discussion of many vitamin phases, including methods for estimating needs, see "Symposium on vitamins", *Lancet*, **63**, 360 (1943). Joliffe, N., *et al.*, *J. Am. Med. Assn.*, **118**, 944 (1942). Kruse, H. D., *Id.*, **121**, 584, 669 (1943).

[89] Williams, R. J., *et al.*, Pub. 4137, Univ. Texas, 1941; *J. Am. Chem. Soc.*, **62**, 175 (1940). Schultz, A. S., *et al.*, *Ind. Eng. Chem.* (*Anal. Ed.*), **14**, 35 (1942); **15**, 141 (1943).

[90] Stock, J., *et al.*, *J. Biol. Chem.*, **150**, 17 (1943).

[91] Snell, E. E., *et al.*, *Ind. Eng. Chem.* (*Anal. Ed.*), **14**, 346 (1939); *J. Biol. Chem.*, **135**, 213 (1940). Shull, G. M., *et al.*, *Id.*, **142**, 913 (1942).

[92] Snell, E. E., and Wright, L. D., *J. Biol. Chem.*, **139**, 675 (1941).

[93] Bessey, O. A., and King, C. G., *J. Biol. Chem.*, **103**, 687 (1933).

[94] Sherman, H. C., *et al.*, *J. Am. Chem. Soc.*, **44**, 165 (1922). See also *Am. J. Pub. Health*, **19**, 1309 (1929); *J. Agr. Res.*, **42**, 35 (1931).

[95] Pharmacopeia of the United States, 1940 (pp. 635–643). Moore, L. A., and Ely, R., *Ind. Eng. Chem.*, **13**, 600 (1941).

[96] Ansbacher, S., *J. Nut.*, **21**, 1 (1941). Almquist, H. J., *Physiol. Rev.*, **21**, 194 (1941).

To sum up, this section discusses briefly the known vitamins important in nutrition, lists and discusses data in tabular form, together with references to the literature on vitamin needs of different species and the influences of several conditions (age, growth rate, etc.) on these needs (see following tables). To render the vitamin needs concretely, one may inspect Tables 20.1 to 20.1e (appendix) showing the dietary standard needs in human nutrition and the composition of some foods in Table 20.2. The following values in relation to the daily standards for a 70-kg (145-lb) person may also be helpful.

Minimum Vitamin A Requirements
(1 I.U. vitamin A = 0.6 mcg β-carotene = 0.21 mcg vitamin A)

Species	Reported requirement		Requirement (mcg/lb. body wt/day)		Ref.
	β-Carotene	Vitamin A	Carotene	Vit. A	
Rat	15–20 mcg/kg/day	4.6–5.3 mcg/kg/day	7–9	2–3	1
Dog		23–43 I.U./kg/wk		2–4	2
Poultry:					
600-g. chick		150 I.U./100 gm feed			3
8 wks. old	125 mcg/100 gm feed		50		4
Chicks	50–100 mcg/100 gm feed	80–160 I.U./100 gm feed	15–30		5
Birth–12 wks.	125–150 mcg/100 gm feed		55–70		6
12 wks. maturity	200 mcg/100 gm feed		50		6
Laying hens	500 mcg/100 gm feed				6
Chicks	125–175 mcg/100 gm feed		30–42		7
Laying hens	450–600 mcg/100 gm feed				7
Turkeys	1000 mcg/100 gm feed				7
Laying hens	2.1 mg/lb. feed				8
Swine	4 mg/100 lbs/day		40		9
	25–39 mcg/kg/day	4.4–6.3 mcg/kg/day	11–18	2–3	1
	30 mcg/kg/day	50 I.U./kg/day	14	5	10
Sheep	25–35 mcg/kg/day	4.3–6.3 mcg/kg/day	11–16	2–3	1
Cattle	26–33 mcg/kg/day	5.1–6.4 mcg/kg/day	11–15	2–3	1
Dairy calves	11 mcg/lb/day		11		11
Reproducing	40–45 mcg/lb/day		40–45		12
Mature	66 mcg/kg/day				11
Horse	20–30 mcg/kg/day	4.2–5.3 mcg/kg/day	9–13	2–3	1
Man		20–30 I.U./kg/day		2–3	13
		25–55 I.U./kg/day		2–3	14

[1] Guilbert, H. R., Howell, C. E., and Hart, G. H., *J. Nut.*, **19**, 91 (1940).
[2] Grimm, P. D., and Short, D. M., *Am. J. Physiol.*, **118**, 477 (1936).
[3] Ringrose, R. C., and Norris, L. C., *Poultry Sci.*, **15**, 390 (1936).
[4] Sherwood, R. M., and Fraps, G. S., Texas Agr. Exp. Sta. Bull. 528, 1936.
[5] Record, P. R., *et al.*, *Poultry Sci.*, **16**, 25 (1937).
[6] Sherwood and Fraps, Texas Agr. Exp. Sta. Bull. 583, 1940.
[7] Sherwood, Proc. 7th Int. World Poultry Congress, page 123, Cleveland, 1939.
[8] Almquist, H. J., and Mecchi, *Poultry Sci.*, **18**, 129 (1939).
[9] Dunlap, G., *J. Agr. Sci. (Engl.)*, **25**, 217 (1939).
[10] Lund, A., *Nut. Abs. and Rev.*, **8**, 894 (1939).
[11] Brande, R., *et al.*, *Biochem, J.*, **35**, 693 (1941); Moore, L. A., *et al.*, *J. Nut.*, **26**, 649 (1943).
[12] Kuhlman, A. H., and Gallup, W. D., *Proc. Am. Soc. An. Prod.*, **33**, 67 (1940).
[13] Booher, L. E., "The vitamins," Am. Med. Ass. p. 111, 1939.
[14] Booher, *et al.*, *J. Nut.*, **17**, 317 (1939).

Vitamin A need: 5000 I.U. a day, about 75 I.U. per kg body weight. A 100 g or 3½ oz portion of beet tops contains about 21,000 I.U. vitamin A (in the form of carotene); spinach 8000 I.U.; mustard greens 11,000 I.U.; carrots 1000 I.U.; squash 1000 I.U.; sweet potato 11,000 I.U.; liver 9000 I.U.; butter 2500 I.U.

Thiamine need: 1.8 to 2.3 mg a day. A serving of 100 g or 3½ oz pork contains about 1.4 mg thiamine, nearly the full daily need, but 100 g fish or poultry supplies only 0.12 gm; 100 g (4 slices) whole-wheat bread supplies about 0.3 mg, but white bread supplies only 0.09 mg; 1 oz dry brewers yeast 1.6 mg; 1 pint milk, 1 oz peanuts, 10 oz oatmeal, 5 oz potatoes, each supplies about 0.22 mg; 1 egg supplies 0.12 mg.

Riboflavin need: 2.2 to 3.3 mg per day. 100 g (3½ oz) portions supply the following amounts of riboflavin: liver 2.5 mg; beef heart 0.7 mg; beef chuck 0.3 mg; fish, as cod or haddock, 0.2 mg; 1 pint milk 1.0 mg; 1 egg 0.2 mg.

Niacin or nicotinic acid need: 15–25 mg per day, 100 g or 3½ oz portions contain the following amounts: liver 20 mg; pork 8 mg; dried brewers yeast 50 mg; beef or fish 6 mg; veal 10 mg; whole-wheat bread 2 mg and white bread 0.75 mg.

Minimum Thiamine Requirements

Species	Reported requirement	Calculated requirement (mcg/100 gm diet)	Ref.
Mouse	10 mcg/mouse/day		1
Rat	80–100 mcg/100 gm diet	80–100	2
	12.5 mcg/rat/day[a]	125–250	3
Chicks	60 mcg/100 gm diet	60	4
Chicks & turkeys	60 mcg/100 gm diet	60	5
Chicks	130–150 mcg/100 gm diet	130–150	6
Dogs:			
Low-fat diet	75 mcg/100 gm diet	75	7
56.5%-fat diet	27.5 mcg/100 gm diet[b]	75	7
Swine	1 mcg/100 lbs/day[c]	50	8
	37 mcg/kg/day		9
	80–94 mcg/100 gm feed[d]	80–94	9
Man	0.22 mg/1000 Calories of diet[e]	88–110	10
Infant	80 units/day		11

[a] It is assumed that a growing rat will eat between 6 and 12 grams of feed daily.

[b] The author of the reference cited based this figure on 100 grams protein and carbohydrate of the high-fat diet

[c] It is assumed that a pig weighing about 100 lbs will consume approximately 2 kg feed per 100 lbs live weight per day.

[d] The authors of this report estimate that their ration contained 75 per cent carbohydrate and protein; using this figure, they conclude that growing pigs require between 106 and 125 mcg thiamine per 100 grams carbohydrate and protein.

[e] It is assumed that 1 gram of diet is equivalent to 4 or 5 Calories.

[1] Houschildt, J. D., *Proc. Soc. Exp. Biol. & Med.*, **49**, 145 (1942).

[2] Arnold, A., and Elvehjem, C. A., *J. Nut.*, **15**, 429 (1938).

[3] Supplee, G. C., *et al.*, *Id.*, **20**, 109 (1940).

[4] Arnold and Elvehjem, *Id.*, **15**, 403 (1938).

[5] "Food and Life," U.S.D. Agr. Yearbook, p. 816, 1939.

[6] Jukes, T. H., and Heitman, H., *J. Nut.*, **19**, 21 (1940).

[7] Arnold and Elvehjem, *Am. J. Physiol.*, **126**, 289 (1939).

[8] Hughes, E. H., *J. Nut.*, **20**, 239 (1940).

[9] Van Etten, C., *et al.*, *Id.*, **20**, 607, 1940.

[10] Williams, R. D., *et al.*, *Arch. Int. Med.*, **69**, 721 (1942).

[11] Knott, E. M., *Proc. Soc. Exp. Biol. & Med.*, **45**, 765 (1940).

Ascorbic acid need: 75 mg a day, approximately 1 mg per kg body weight. ½ grapefruit (7 oz) contains 80 mg; 1 orange (5.5 oz) 75 mg; 100 g fresh raw cabbage 80 mg; 100 g lettuce 15 mg; 100 g green pepper 170 mg; 100 g tomatoes 30 mg; 100 g lemon, grapefruit, orange, or tangerine 45 mg; 100 g or 100 cc juice of lemon, grapefruit, or orange 40 to 50 mg; 100 g peeling of lemon, grapefruit, or orange 200 mg; 100 g turnip or potato 30 mg; 100 g carrots 7 mg.

20.6. Vitamins in relation to the neuro-endocrine and neuro-muscular systems. The relation of vitamins to the nervous system is of particular human interest not only because the mental condition in man is particularly important, but also because man manifests certain mental disorders not shown clearly or investigated conveniently in laboratory or farm animals. This is, of course, due to the high development of the human brain (Fig. 10.1, and Sect. 10.9), affording a favorable substrate for the development of mental disorders, to the relatively slow growth rate (Ch. 16) and long life span (Chs. 18 and 19), which permit slow-acting nutritional deficiencies to produce pronounced nervous and mental effects.

Estimated Riboflavin Requirements

Species	Reported requirement	Requirement calculated to mcg/100 gm feed	Reference
Rat	10 mcg/rat/day[a] 18 mcg/rat/day[b]	80–160 144–288	1 2
Poultry:			
Chicks	290 mcg/100 gm feed[c]	290	3
Chicks	60 Sherman units/100 gm feed	150	4
Chicks	100–350 mcg/100 gm feed	100–350	5
Chicks	190–200 mcg/100 gm feed	190–200	6
Hens	230 mcg/100 gm feed	230	3
Egg production	100–130 mcg/100 gm feed	100–130	7
Hatchable eggs	245 mcg/100 gm feed	245	7
	2.5 mg/lb. feed	573	8
	220–230 mcg/100 gm feed	220–230	6
Dog	200–400 mcg/100 gm feed[d] 11.3 mcg/lb/day	200–400	9 10
Swine	1–3 mg/100 lb/day[e]	50–150	11
Man	35–60 mcg/kg/day[f]		12

[a] It is assumed that a growing rat will eat about 6–12 gm feed daily. The value 10 mcg/day was not reported as a minimum requirement; it merely represents the level fed in a purified diet which was used in studying a deficiency of pyridoxine.

[b] It is again assumed that a young rat will consume about 6–12 gm. feed daily. The value 18 mcg/day was the minimum amount of riboflavin which would support normal growth on a low-fat diet; it was not enough to support growth on a high-fat diet.

[c] 1 mcg = 0.4 Bourquin-Sherman Unit.

[d] Judging from Elvehjem's data and the fact that he fed the supplement only once a week, it is believed that the minimum riboflavin requirement of the dog is nearer to 200 than to 400 mcg/100 gm feed.

[e] It is assumed that a pig will eat about 2 kilograms of feed per 100 lbs live weight per day.

[f] These values for man are based on the amount necessary to maintain normal levels of riboflavin in the urine. Sebrell states that the minimum daily requirement is nearer to 35 than to 60 mcg per kilogram of body weight.

[1] Supplee, G. C., *et al.*, *J. Nut.*, **20**, 109 (1940).

[2] Mannering, G. J., *et al.*, *Proc. Soc. Exp. Biol. & Med.*, **46**, 100 (1941).

[3] Norris, L. C., *et al.*, Cornell Agr. Exp. Sta. Bull. 660, 1936.

[4] Jukes, T. H., *Poultry Sci.*, **17**, 227 (1938).

[5] Heuser, G. F., *et al.*, *Id.*, **17**, 105 (1938)

[6] Hunt, C. H., *et al.*, *Id.*, **18**, 330 (1939).

[7] Davis, H. J., *et al.*, *Id.*, **17**, 87 (1938).

[8] Lepkovsky, S., *et al.*, *Hilgardia*, **11**, 571 (1938).

[9] Axelrod A. E., *et al.*, *Am. J. Physiol.*, **128**, 703 (1939).

[10] Street, H. R., and Cowgill, G. R., *Am. J. Physiol.*, **125**, 323 (1937).

[11] Hughes, E. H., *J. Nut.*, **20**, 233 (1940).

[12] Sebrell, W. H. *et al.*, *Public Health Repts.*, **56**, 510 (1941).

Because of their intimate integrative effects on the organism as a whole, it is often difficult to separate nervous from endocrine disorders. For instance, as shown by Pavlov, Cannon, Crile, and younger contemporaries, the nervous system acts on the adrenals, thyroid, pituitary, gonads, islets of Langerhans, and other glands, and the secretions of these glands in turn act on the nervous system, in a sort of a circle, sometimes (in disease) in a vicious circle (Sects 10.8 and 18.2.3).

The dietary influence on the endocrines may be of specific or general nature. For instance, iodine deficiency leads to various thyroid abnormalities, ranging from relatively harmless goiter to hopeless cretinism[97]. This is understandable, since iodine constitutes 65 per cent of the thyroid hormone. Some excess iodide intake is, on the other hand, harmless; it is excreted. Less specific are the thyroid hypertrophy in vitamin A deficiency (McCarrison, Sure), and thyroid depression [including depression of the metabolism accelerating effect of thyroxine (Drill, Drummond)] in vitamin A excess[97].

Nicotinic Acid (Niacin) Requirements

Species	Reported requirement	Reference
Dog	0.2–0.5 mg/kg/day	1
	0.5–1.5 mg/kg/day	2
	10 mg semi-weekly[a]	3
	0.25 mg/kg/day	4
Monkey	2.5 mg/kg/day	5
Swine	13.7 mg/100 lbs/day[b]	6
	2 mg/kg/day[b]	7

[a] The dog used in this experiment weighed 7.25 kg.

[b] These values for swine represent levels of niacin fed as supplements to a purified diet and do not necessarily represent the minimum requirement for swine.

[1] Margolis, G., *et al.*, *J. Nut.*, **16**, 541 (1938).
[2] Elvehjem, C. A., *et al.*, *J. Biol. Chem.*, **123**, 137 (1938).
[3] Sebrell, W. H., *J. Nut.*, **16**, 355 (1938).
[4] Birch, T. W., *Id.*, **17**, 281 (1939).
[5] Harris, L. J., *Biochem. J.*, **32**, 1479 (1938).
[6] Hughes, E. H., *Hilgardia*, **11**, 595 (1939).
[7] Wintrobe, M. M., *Am. J. Physiol.*, **126**, 375 (1939).

Pantothenic Acid Requirements

Species	Reported requirement	Reference
Mouse	30 mcg/day[a]	1
Rat	80 mcg/day[b]	2
	100 mcg/day[b]	3
	100 mcg/day	4
	50–75 mcg/day	5
	100 mcg/day at 3 weeks of age	6
	25 mcg/day at 10 weeks of age	6
Chick	1.4 mg/100 gm feed	7
	600 mcg/100 gm feed[c]	8
Dog	100 mcg/kg/day[d]	9
Swine	7.8–11.8 mg/100 lb/day[b]	10

[a] For growth of mice from 10 to 20 grams.

[b] For growth.

[c] A slight diffence in the requirement for pantothenic acid was observed in different breeds.

[d] This amount is for growth; much less is required for adult animals.

[1] Sandza, J. G., and Cerecede, L. R., *J. Nut.*, **21**, 609 (1941).
[2] Unna, K., *J. Nut.*, **20**, 565 (1940).
[3] Henderson, L. M., *et al.*, *Id.*, **23**, 47 (1942).
[4] Daft, F. S., *et al.*, *Public Health Reports*, **55**, 1333 (1940).
[5] György, P., and Poling, C. E., *Science*, **92**, 202 (1940).
[6] Unna and Richards, G. V., *J. Nut.*, **23**, 545 (1942).
[7] Jukes, T. H., *J. Biol. Chem.*, **129**, 225 (1939).
[8] Bauernveind, J. C., *Poultry Sci.*, **21**, 142 (1942).
[9] Schaefer, A. E., *et al.*, *J. Biol. Chem.*, **143**, 321 (1942).
[10] Hughes, E. H., and Ittner, N. R., *J. Animal Sci.*, **1**, 116 (1942).

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[97] See Section 7.3.2A for the literature.

Ascorbic acid also affects the thyroid. Massive ascorbic acid depresses the metabolism-accelerating effect of thyroxine (Belasco and Murlin), and ascorbic-acid deficiency (in guinea pigs) hypertrophies the thyroid with hemorrhagic infiltrations and affects adrenocortical hormone production.

A curious effect of thyroid is that in its absence carotene cannot be converted into vitamin A. While normal herbivors fed good roughage do not suffer from vitamin A deficiency because they utilize the carotene in the roughage, thyroidectomized herbivors develop serious lack of A on good roughage.

It would, then, appear that hyperthyroidism and Graves disease would be ameliorated by massive doses of ascorbic acid and vitamin A, especially since hyperthyroidism tends to damage the liver and thus interfere with vitamin A storage, and that hypothyroid individuals, not able to utilize carotene, should be fed vitamin A as such (not carotene).

Since thyroxine accelerates the metabolic rate of all nutrients, including vitamins, the accelerated metabolism of hyperthyroidism is likely to develop into dietary deficiency for some nutrient consumed at a relatively low level. This special deficiency may mask or confuse the thyroid abnormality. For instance, the high pulse rate associated with hyperthyroidism may be confused with or masked by the low pulse rate associated with thiamine deficiency.

Similarly, vitamin D and calcium deficiency may be the outstanding symptoms in hyperthyroidism since, under the influence of thyroxine, the rate of calcium catabolism tends to parallel that of energy and nitrogen metabolism.

One of the very interesting relations between an endocrine and a vitamin is that between the parathyroid and vitamin D, both of which are regulators of calcium and phosphorus metabolism, but in different ways (Sect. 7.5). While the primary function of the parathyroid is to maintain constant the blood-calcium level, that of vitamin D is to catalyze calcium assimilation into bone. The parathyroid weight increases with increase in calcium demands. Thus while the parathyroid weight of a non-milking goat is 100 mg, that of a milking goat is 170 mg[98]. Animals without parathyroids, on the other hand, may be maintained indefinitely by high calcium and vitamin D intake, and the same holds true for high-milking dairy cows (when the parathyroid may not be able to meet the demands made on it) which may be maintained in good calcium condition, avoiding milk fever, by high calcium and vitamin D intake (Sect. 7.5).

Vitamin E deficiency, if severe enough, leads to such atrophy of the anterior pituitary (in rats) as to amount to virtual hypophysectomy as regards reproduction[99].

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[98] Campbell, I. L., and Turner, C. W., Univ. Missouri Agr. Exp. Sta. Res. Bull. 353, 1942.

Vitamin E deficiency also leads to nutritional muscular dystrophy, and a spastic ataxia-like paralysis in guinea pigs and rabbits[100], and to nutritional encephalomalacia in chicks[101], characterized by Parkinsonian-like tremors and head retraction and rotation. It has been known[102] since 1928 that the lack of a dietary factor (present in wheat-germ oil) leads to degenerative changes in the neuro-skeletal system.

Cod-liver oil appears to have something that counteracts the anti-paralysis action of vitamin E[103]. The apparently injurious effect of cod-liver oil on herbivora[104] may be due to an "antagonism" between E and some anti-vitamin E factor in the oil; or, when rancid, it may destroy the vitamin E by autoxidation[104a].

While what is now called thiamine deficiency was the first to be investigated in relation to nervous function[105] (in 1897 Eijkmann published his report on polyneuritis in chickens[106] and in 1911 Funk prepared the beriberi-curative substance from rice polishing and called it vitamine), perhaps all B vitamins involved in carbohydrate metabolism are needed for normal nervous function because the nervous system, particularly the brain, apparently obtains its energy from oxidation of carbohydrate alone[107]. Even diabetics not receiving insulin have a brain R.Q. which is virtually unity[108], indicating that the brain always obtains its energy from carbohydrate oxidation. Since, therefore, the function of the nervous system depends on the energy supplied by carbohydrate with the aid of catalysts involving certain vitamins as prosthetic groups, it is obvious that deficiency of vitamins, which interferes with carbohydrate oxidation[109], will lead to dysfunction of the nervous system. It has, indeed, been shown that the arterio-venous oxygen difference is about 25 per cent lower and the arterio-venous sugar difference is about 60 per cent higher in persons suffering from severe vitamin B complex deficiency (pellagra) than in normal persons[110]. As the deficiency progresses, various nervous and psychic manifestations follow, such as neuritis, neuralgia, nervousness, anxiety, fatigue, mental confusion, and so on, and perhaps also such diseases as migraine and sciatica. The longer the period on the deficient diet, the more severe the dysfunction. The ataxia-like Vernicke's syndrome in man (due to alcoholism), or Chastek paralysis in foxes[110a], is apparently an advanced state of thiamine deficiency.

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[99] See Section 6.4.3; also Barrie, M. O., *Nature*, **139**, 287 (1938); Singer, E., *J. Physiol.*, **87**, 287 (1936).

[100] Goettsch, M., and Pappenheimer, A. M., *J. Exp. Med.*, **54**, 145 (1931).

[101] Pappenheimer and Goettsch, *Id.*, **53**, 11 (1931).

[102] Evans, H. M., and Bishop, K. S., *J. Med. Res.*, **3**, 233 (1923). Sure, B., *J. Biol. Chem.*, **58**, 693 (1923–24). Evans, H. M., and Burr, G. O., *Id.*, **76**, 273 (1928). Evans, *et al.*, *J. Nut.*, **19**, 547 (1940). Mason, K., *et al.*, *Proc. Am. Physiol. Soc.*, 43rd meeting, 1941.

[103] Mackenzie, C. G., and J. B., and McCollum, E. V., *Science*, **94**, 216 (1941).

[104] McCay, C. M., *et al.*, Cornell Univ. Agr. Exp. Sta. Memoirs 178 and 217, 1935–38.

[104a] Mattill, H. A., and Columbic, C., *J. Nut.*, **23**, 625 (1942). Morgulis, S., *Id.*, p. 473. Dam, H., *Id.*, **27**, 193 (1944) thinks that it is the cod liver fatty acids that damage the tissues.

[105] For an excellent monograph on these problems, see Cobb, S., Gildea, E. F., and Zimmerman, H M., editors: "The role of nutritional deficiency in nervous and mental disease", Williams & Wilkins, 1943. See also ref. 88.

[106] For references to the literature not here cited, see Sect. 6.4.3.

[107] Himwich, H. E., and Nahum, L. H., *Am. J. Physiol.*, **99**, 389 (1930).

[108] Himwich, and Nahum, *Id.*, **90**, 389 (1929); **101**, 446 (1932).

[109] Banga, I. L., Ochoa, S., and Peters, R. A., *Bioc. J.*, **33**, 1109 (1939).

[110] Spies, T. D., *et al.*, *Am. J. Med. Sci.*, **199**, 199, 840, 849 (1940).

As previously explained (Ch. 3 and 6) energy is required to maintain the integrity of living tissue, and when this maintenance energy is not available, the tissue disintegrates. Nervous tissue is particularly sensitive to deficiency of maintenance energy, as indicated dramatically by the "black out" in high-altitude flying as result of brief oxygen deficiency, and it is reasonable to assume that the deficiency of a limiting vitamin involved in carbohydrate oxidation may lead to injury, depending on the severity and duration of deficiency. This appears to be certain as regards deficiency of thiamine[111], riboflavin[111, 112], pyridoxine[112, 113], and nicotinic acid[114], all of which are of great clinical importance.

Vitamin A deficiency may lead to generalized peripheral nerve lesions[115] (Fig. 20.6). It is, however, believed[116] that the injury to the nervous system by vitamin A deficiency in early life may be not directly on the nerves but by retarding skeletal growth; this leads to injury of the nervous system by undue crowding, or similar mechanisms. Thus Moore[117] observed a constriction of the optic foramen and, therefore, of the optic nerve, with consequent blindness, in vitamin A-deficient calves. Vitamin A deficiency may similarly lead to increased intracranial pressure with associated disorders of the central nervous system and of behavior.

Summing up, it appears that some endocrine, nervous, mental, and muscular disorders, including "shifting pains", may be associated with disturbed intermediate metabolism as result of deficiency of vitamins, particularly of thiamine, nicotinic acid, pyridoxine, and riboflavin, and by different mechanisms as result of deficiency of vitamins A, E, D, and biotin.

20.7. Amino acid relations in nutrition[118]. It has been explained (Sect. 20.1) that species differ as regards dependence on their diet for vitamins, because some vitamins are synthesized by microorganisms in the digestive tract, some are synthesized by body tissue, and some apparently do not need certain vitamins for their metabolic processes[119]. The situation is similar as regards amino acids. Ruminants appear to be more or less independent of dietary amino acids because, like the B-vitamins, amino acids are synthesized from simpler nitrogen compounds by rumen microorganisms (Sect. 20.1). This discussion is, therefore, necessarily concerned with nonruminants, mostly rats and mice, because the experimental work was practically confined to these species.

[110a] Green, R. G., *et al.*, *J. Nut.*, **21**, 243 (1941); *Am. J. Path.*, **18**, 79 (1942). Joliffe, N., *et al.*, *Q. J. Alcohol*, **2**, 73 (1941).

[111] Zimmerman, H. M., *et al.*, *Arch. Path.*, 13, 207 (1932); *J. Exp. Med.*, **59**, 21 (1934); *Am. J. Physiol.*, **109**, 440 (1934); *Yale J. Biol. Med.*, **12**, 23 (1939). Alexander, L., *Am. J. Path.*, **16**, 61 (1940).

[112] Lillie, R. D., and Sebrell, W. H., Nat. Inst. Health Bull. 162, 1933.

[113] Street, H. R., Cowgill, G. R., and Zimmerman, H. M., *J. Nut.*, 21, 275 (1941); **22**, 7 (1941). Joliffe, N., *J. Am. Med. Assn.*, **117**, 1496 (1941).

[114] Joliffe[113]. Wortis, H., *Psychiat. Quart.*, **15**, 693 (1941).

[115] Zimmerman, H. M., *J. Exp. Med.*, **57**, 215 (1933).

[116] Wolbach, S. B., and Bessey, O. A., "Tissue changes in vitamin deficiencies", *Physiol. Rev.*, **22**, 233 (1942).

[117] Moore, L. A., *J. Nut.*, **17**, 443 (1939); **26**, 649 (1943).

[118] For extensive discussion of the amino acid and protein literature, see Mitchell, H. H., and Hamilton, T. S., "The biochemistry of amino acids", Reinhold Pub. Corp., New York, 1929. Schmidt, C. L. A., ed., "The chemistry of amino acids and proteins", 1938, and "Addendum, the chemistry of amino acids and proteins", C. C. Thomas, Springfield, Ill., 1943.

About 1907 Wilcock and Hopkins[120] observed that mice lose weight when the dietary protein is confined to zein (from corn) unless supplemented by tryptophane. About 1912 Osborne and Mendel[121] demonstrated that rats whose only source of protein was zein were definitely dependent for their growth on lysine as well as on typtophane supplements. Quite recently Rose[122] and associates demonstrated that threonine and methionine are essential amino acids (Fig. 20.5). And now it is believed that (for growth of rats) 9 amino acids are absolutely indispensable, 9 are dispensable, and 4 are partly dispensable. The meaning of "partly dispensable" is illustrated by arginine[123], which is synthesized in the body but at a relatively slower rate than are the other dispensable amino acids. The same is true of glycine for chickens[123a]. The dispensable ones are synthesized by the body or by gut bacteria.

It is believed that methionine can replace cystine, at least in part, but that cystine cannot replace methionine[124]; yet cystine appears to be a limiting factor in the growth of animals in which (cystine-rich) hair is a major part of the growth, such as for growth of sheep wool[125] and rat hair[126], which contain 13 per cent cystine and 0.5 per cent methionine. Certain cystine-poor proteins, such as casein and white-bean protein, which contain methionine, do not support satisfactory growth without the addition of cystine.

The dietary essential amino acid needs undoubtedly vary with the essential amino-acid composition of the body tissues. Roughly speaking, half of the muscle protein is composed of the essential amino acids and contains[127] 8 to 9 per cent lysine, 6 to 8 per cent arginine, 4 to 5 per cent each of threonine, serine, tyrosine, and phenylalanine, 3 to 4 per cent methionine, 1.8 to 2.4 per cent histidine, 1.1 to 1.4 per cent cystine, 1.2 to 1.4 per cent trypto-

[119] For review of the literature on interrelations between the replaceability of the vitamins by amino acids, such as that alanine can replace pyridoxine, see *Nut. Rev.*, **2**, 99 (1944).

[120] Wilcock, E. G., and Hopkins, F. G., *J. Physiol.*, **35**, 88 (1906–7).

[121] Osborne, T. B., and Mendel, L. B., *J. Biol. Chem.*, **17**, 315 (1914); **12**, 473 (1912); **20**, 351 (1915); **26**, 1 (1916). "Feeding experiments with isolated food substances", Carnegie Inst. of Wash. Publ. 156, Parts I and II, 1911.

[122] McCoy, R. H., Meyer, C. E., and Rose, W. C., *J. Biol. Chem.*, **112**, 291 (1935). Rose, W. C., *J. Biol. Chem.*, **26**, 521 (1936).

[123] Rose, W. C., *Physiol. Rev.*, **18**, 109 (1938).

[123a] Almquist, H. J., *Am. Soc. Exp. Biol., Fed. Proc.*, **1**, 269 (1924).

[124] Rose, W. C., *et al.*, *J. Biol. Chem.*, **121**, 403 (1937).

[125] Marston, H. R., *J. Agr. Sci.*, **25**, 113 (1935).

[126] Smuts, D. B., Mitchell, H. H., and Hamilton, T. S., *J. Biol. Chem.*, **95**, 283 (1932).

[127] Beach, E. F., Munks, B., and Robinson, A. R., *J. Biol. Chem.*, **148**, 431 (1943).

phane. It works out that for every 10 molecules of lysine there are in the muscle tissue approximately 9 of serine, 7 each of arginine and threonine, 4 each of phenylalanine and tyrosine, 3.5 of methionine, 2.5 of histidine, and about 1 each of tryptophane and cystine. The visceral organs (in contrast to muscle) contain less lysine, more cystine, serine, phenylalanine and tryptophane.

The three categories of amino acids—indispensable, dispensable, and partly dispensable—are listed in the following table. The numerals in parentheses indicate the proportions of the indispensable amino acids (active form) required to support growth in rats fed at certain levels[128].

Three amino acid categories.

Nutritionally indispensable (for rats)		Partly dispensable		Dispensable
Tryptophane	(0.2)	Arginine	(0.2)	Alanine
Lysine	(1.0)	Cystine		Glutamic acid
Phenylalanine	(0.7)	Tyrosine		Hydroxyglutamic acid
Histidine	(0.4)	Glycine		Aspartic acid
Threonine	(0.6)			Serine
Methionine	(0.6)			Proline
Leucin	(0.9)			Hydroxyproline
Isoleucin	(0.5)			Citrulline
Valine	(0.7)			Norleucine

The following numerical estimates[129] of the amino acids, in several food proteins are instructive.

Percentage amino acid make-up of meat, milk, eggs, and related food proteins.

Amino Acid	Meat	Milk	Casein	Egg	Wheat	Wheat germ	Yeast	Soybean
Leucine	12	15	12	19	13	7.0	13	8
Lysine	8.1	7.5	6.9	6.0	2.7	5.5	6.0	5.4
Arginine	7.1	4.3	4.1	7.0	3.0	6	4.3	5.8
Phenylalanine	4–5	5.7	5.2	5.6	8.7	4.2	4.1	5.3
Threonine	4.3	4.6	3.9	4.9	3.3	3.8	5.0	4.0
Valine	3–4	5	7	4–5	3–4	3–5	4–5	4–5
Isoleucine	3.4	4.4	5	5.3	4	3	3–4	4
Methionine	3.3	2.8	3.5	4	3.0	2.0	2	1.8
Tyrosine	3.1	5.3	6.4	5.0	3.8	3.8	4.2	4.1
Histidine	2.2	2.5	2.5	2.4	1–2	2.5	2.8	2.3
Tryptophane	1.2	1.6	1.5	1.6	1	1.0	1.4	1.5
Cystine	1.1	1.1	0.4	2.1	1.3	1	1.3	0.6

A given amino acid, or an amino-acid derivative, may be particularly important in one but not in another metabolic process. Thus, according to

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[128] This problem is still under investigation and debate. See, for example, Kinsey, and Grant[87].

[129] Block, R. J., and Bolling, D., *J. Am. Diet. Assn.*, **20**, 69 (1944).

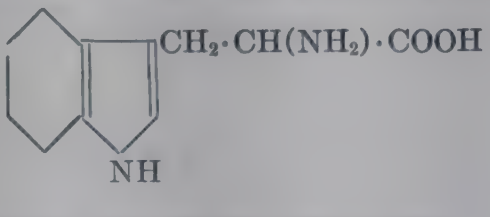
Hammett[130], histidine is particularly useful in maintenance (rather than growth); sulfhydryl in cell proliferation (rather than maintenance); proline in cell differentiation (rather than proliferation); arginine in growth initiation; adenine and guanine in cell segregation (organization); the alpha amino acids in increase of cytoplasmic mass.

There are obvious difficulties in precise apportioning of amino-acid functions because of the intimacy between the several growth sequences. For instance, a given amino-acid necessary for maintenance must also be necessary for growth, since there can be no growth without maintenance.

What was said about the effects of vitamin deficiency is applicable to amino-acid deficiency, as the amino acids also enter into the building of various "carriers" from hemoglobin to enzymes.

The amino acids are characterized by their amino group, NH_2. The amino acids are usually divided into the following classes.

1. Monocarboxylic amino acids: glycine, alanine, valine, isoleucine, norleucine
   Typical formula: $CH_3 \cdot NH_2 \cdot COOH$, glycine or amino acetic acid
   $CH_3 \cdot CHNH_2 \cdot COOH$, alanine or α-amino propionic acid
2. Dicarboxylic amino acids: aspartic acid, glutamic acid
   Typical formula: $HOOC \cdot CH_2 \cdot CH_2 \cdot CHNH_2 \cdot COOH$, glutamic acid or α-amino glutaric acid
3. Hydroxyamino acids: serine, threonine, hydroxyglutamic acid
   Typical formula: $CH_2 \cdot CHOH \cdot CHNH_2 \cdot COOH$, threonine or α-amino β-hydroxybutyric acid
4. Aromatic amino acids: phenylalanine, tyrosine
   Typical formulas: $C_6H_5 \cdot CH_2 \cdot CHNH_2 \cdot COOH$, phenylalanine or α-aminophenylpropionic acid
   $HO \cdot C_6H_4 \cdot CH_2 \cdot CHNH_2 \cdot COOH$, tyrosine or α-amino β-ρ-hydroxphenyl-propionic acid
5. Indole amino acid: tryptophane, β-indole-γ-amino-propionic acid has the formula:



6. Sulfur-containing amino acids: cystine, methionine.
7. Basic amino acids: lysine, histidine, arginine:
   Typical formula: $H_2N \cdot (CH_2)_4 \cdot CHNH_2 \cdot COOH$, lysine
8. Pyrrole-containing amino acids: proline, hydroxyproline

Since the value of a protein depends on its amino acids, the designation "crude protein" (rather than "true protein") is used in feed analysis. This includes all nitrogen multiplied by 6.25 (assuming that protein contains 16 per cent N, so that $100/16 = 6.25$). The non-protein nitrogen is not all peptide and amino acid, but only roughages, as alfalfa, are heavily loaded with non-amino nitrogen[131], which is utilized by ruminants.

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[130] Hammett, F. S., *Growth*, **6**, 59 (1942).

[131] Jones, D. B., "Factors for converting percentages of nitrogen in foods and feeds into percentages of protein", U. S. Dept. Agr. Circ. 183, 1931. Hart, E. B., and Bentley, W. H., "Water-soluble nitrogen in feeding stuffs", *J. Biol. Chem.*, **22**, 477 (1915).

As previously noted (Sect. 20.4), if one of the essential amino acids is lacking, the other amino acids cannot be used for protein building, with the result that they are deaminized and the nitrogen is eliminated with the associated "specific dynamic effect" (Ch. 4). The non-nitrogen residue (lactic acid, pyruvic acid, pyruvic aldehyde) may be transformed into sugar as indicated by the following diagrammatic equations (Sect. 6.3).

$$\underset{\textit{alanine}}{CH_3\cdot CH(NH_2)\cdot COOH} \xrightarrow[\text{hydrolytic}\atop\text{deamination}]{} NH_3 + \underset{\textit{lactic acid}}{CH_3\cdot CHOH\cdot COOH} \rightarrow \underset{\textit{urea}}{OC(NH_2)_2} \underset{}{+} \underset{\textit{sugar}}{C_6H_{12}O_6}$$

$$CH_3\cdot CH(NH_2)\cdot COOH + O \xrightarrow[\text{oxidative}\atop\text{deamination}]{} NH_3 + \underset{\textit{pyruvic acid}}{CH_3\cdot CO\cdot COOH} \rightarrow \text{urea} + \text{sugar}$$

$$CH_3\cdot CH(NH_2)\cdot COOH \xrightarrow[\text{simple}\atop\text{deamination}]{} NH_3 + \underset{\textit{pyruvic aldehyde}}{CH_3\cdot CO\cdot CHO} \rightarrow \text{urea} + \text{sugar}$$

The urea is eliminated and the sugar is retained.

Under certain conditions these reactions are reversed, and alanine is formed from lactic acid and pyruvic aldehyde. This may explain the production of the dietary dispensable amino acid in the body (Sect. 6.5). There are always NH_3 compounds and carbohydrate intermediate compounds in the body from which such amino acids may be produced. Moreover, glycerol ($CH_2OH\cdot CHOH\cdot CH_2OH$, from dietary fat) is related, through glyceraldehyde ($CH_2OH\cdot CHOH\cdot CHO$), to pyruvic aldehyde ($CH_3\cdot CO\cdot CHO$). These relations indicate the possibilities of amino acid synthesis in the body from NH_3 compounds and carbohydrate (α-hydroxy-acids as lactic acid, α-ketonic acid as pyruvic aldehyde); these relations also indicate how under certain conditions protein is converted to carbohydrate[132, 133] (up to 58 per cent) and how fat is converted to carbohydrate[134].

The nutritional value of the digestible part of a protein when fed at a low level, depends on the proportion of the essential and semi-essential amino acids in the food in relation to the proportions required by the body. As explained previously (Sect. 20.4), the supplementary value of proteins is their ability to supplement each other's deficiencies. For instance, the nutritional value of grain protein is increased by the addition of milk because the amino acids in milk protein make good the amino-acid deficiencies in grain protein; the unfavorable influence of heat on some proteins is due to the injury of a limiting amino acid, and so on.

There are many empirical methods of representing the numerical value of protein, some of which were discussed in Sect. 20.3. The writer likes the method of McCollum and Parsons (eq. 20.3), which represents the protein value in terms of the ratio of nitrogen retained to nitrogen consumed under a given set of conditions. Another interesting way of representing the protein value is in terms of some standard protein value. It has been suggested[135] that the value of proteins be expressed in terms of milk-protein replacement values.

Thomas[136] and more recently Mitchell[137] defined the nutritive value of protein in terms of "*biologic value*", *the percentage of absorbed (from the digestive tract) nitrogen which is retained, that is, which is not excreted in the urine as exogenous nitrogen.* This

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[132] Rapport, D., "The interconversion of the major foodstuffs", *Physiol. Rev.*, **10**, 349 (1930).

[133] Lusk, G., "The science of nutrition", 1928.

[134] Mitchell, H. H., "The possibility of the conversion of fatty acids to glucose in the animal body", *J. Nut.*, **6**, 473 (1933); **22**, 167, 183 (1941).

[135] Murlin, J. R., and Mattill, H. A., *J. Nut.*, **16**, 15, 249 (1938).

[136] Thomas, K., *Arch. Anat. Physiol.*, p. 219, 1909.

[137] Mitchell, H. H., *J. Biol. Chem.*, **58**, 873 (1924).

concept is more complex than appears. In the first place the biological value of protein as thus defined may be only remotely related to its actual nutritional value. For instance, wool, hair, feathers may have a high biological value but no real nutritional value because of the insignificant digestibility of wool, hair, and feathers; the biological value of protein is not concerned with digestibility, but only with the retention of that part of the protein which is digested and absorbed into the body proper. Thus, cocoa protein and navy-bean protein have[138] the same biological value, 38 per cent; but since the digestibility of cooked navy-bean protein (76 per cent) is twice that of cocoa protein (38 per cent), the real nutritional value of cooked navy-bean protein is twice (29 per cent) that of cocoa protein (14 per cent) in spite of the same biological value. Proteins, such as zein, on the other hand, are highly digestible but lack lysine and tryptophane; so is gelatin, which lacks tryptophane. But McCollum's definition takes care of both digestibility and amino-acid balance.

Protein Values of Foods for Maintenance and Growth: Level of Protein Feeding, 8 to 10 per cent.
(From Mitchell and Hamilton, except last column.)

Food	Water Content[1] %	Protein Content[1]		Quality of Protein		Metabolic Protein in Feces		Net Protein Value of Food		Net Protein Value of Protein[4] %
		On Fresh Basis %	On Dry Basis %	Digestibility (corr.[2]) %	Biological Value %	On Fresh Food Basis %	On Dry Food Basis %	On Fresh Basis %	On Dry Basis %	
Whole egg	73.2	13.2	49.3	100	94	0.4	1.4	12.0	44.9	94
Milk	87.0	3.3	25.4	100	85	0.2	1.4	2.6	20.2	85
Egg white[3]	86.2	12.3	89.1	100	83	0.2	1.4	10.0	72.6	83
Beef liver	71.2	20.4	70.8	90	77	0.4	1.4	14.9	51.1	69
Beef kidney	76.7	16.6	71.3	99	77	0.3	1.4	12.3	52.8	76
Beef heart	62.6	16.0	42.8	100	74	0.5	1.4	11.3	30.3	74
Beef round	70.0	21.3	71.0	96	69	0.4	1.4	13.7	45.7	66
Pork ham	60.0	25.0	62.5	100	74	0.6	1.4	17.9	44.8	74
Veal	73.4	20.7	78.0	100	62	0.4	1.4	12.4	47.0	62
Rolled oats	7.7	16.7	18.1	90	65	1.3	1.4	9.8	10.6	59
Whole wheat	11.4	13.8	15.6	91	67	1.3	1.4	7.1	8.1	61
White flour	12.8	10.8	12.4	100	52	1.3	1.4	4.3	5.0	52
Whole corn	10.3	7.5	8.4	95	60	1.3	1.4	3.0	3.5	57
Potato	78.3	2.2	10.1	78	67	1.3	1.4	0.8	3.9	52
Navy beans[3]	12.6	22.5	25.7	76	38	1.3	1.4	4.2	6.0	29
Cocoa	4.6	21.6	22.6	38	37	1.4	1.4	1.6	1.8	14
Chocolate	5.9	12.9	13.7	38	37	1.4	1.4	0.4	0.6	14

[1] Average analyses taken, as far as possible, from Bull. 28 (revised), Office of Experiment Stations, U. S. Dept. Agr.

[2] The metabolic nitrogen in the feces is assumed to equal 0.23 gram per 100 grams of dry matter of food. See Bull. Natl. Research Council, 1926, xi, pt. 1, no. 55, p. 23.

[3] Cooked.

[4] Product of digestibility and biological value of the protein, assumed to represent the percentage of the intake protein retained for maintenance or growth.

Mitchell and Hamilton also employed McCollum's definition but called it "net protein value", comparable to the net energy value of feed (Sect. 2.3) illustrated in the following statement and table from these authors[138].

> A cut of lean-beef round contains 21.3 per cent protein, 96 per cent of which is "really" digestible (that is, not including the metabolic nitrogen in the feces with the indigestible material). Hence, this beef round contains 0.96 × 21.3 = 20.4 per cent *digestible* protein. When this meat is fed to rats at 8 to 10 per cent protein level in the diet, its biological value is 69 per cent; hence the net protein value of this cut of meat is 0.69 × 20.4 = 14.1 per cent. A part of the metabolic nitrogen (that part related to the amount of food

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[138] Mitchell, H. H., and Hamilton, T. S., "The biochemistry of amino acids", Reinhold Pub. Corp., pp. 555-556, 1929.

intake) in the feces may be charged to this "net protein". Mitchell assumes that the metabolic nitrogen in feces is of the order of 0.23 g, or the protein equivalent is 1.4 g per 100 g of dry food consumed. If the dry matter in the fresh meat is 30 per cent, then the metabolic nitrogen in the feces is $0.3 \times 1.4 = 0.4$ per cent. The final net protein value is then $14.1 - 0.4 = 13.7$ per cent of the fresh meat. This is the maximum percentage of protein ($6.25 \times N$) in the food which is available for maintenance or productive purposes. The foregoing table is from Mitchell and Hamilton (p. 779). We added the last column on the right side of the table to represent the net protein value of the protein, which is the product of the "biological value" and the "true digestibility" of the protein. "True digestibility" is the difference between the fecal N (called metabolic N) on a low protein diet and the fecal N on the experimental diet.

The problem of evaluating the various categories of urinary and fecal nitrogen, together with the cogent literature[135, 139, 140], are discussed in Sections 13.1 and 14.9.

The protein needs in relation to body size in different species were previously discussed (Ch. 15), and the needs for adult man, about 70 g a day for a 70-kg person, are indicated in Table 20.1. To make this value concrete, one may note that per serving (100 g or 3½ oz), meat, poultry, or fish contains about 17 g protein, enough to supply a fourth of the day's need; a pint of milk contains about 16 g; 4 slices (100 g) whole-wheat bread contains about 10 g protein (white bread contains 8 to 9 g); an egg contains about 6.7 g protein. Per pound, meat, fish, or poultry contains 66 g protein; dry legumes and nuts 97 g; grain products 40 g; leafy vegetables 6 g; potatoes 8 g; dried fruits 13 g.

20.8. Notes on mineral relations in nutrition. The average mature human body contains the equivalent of about 5 per cent ash, equivalent to about 6 lb ash, which comes from and returns to the earth. The percentage composition of this ash is approximately: calcium 40, phosphorus 22, potassium 5, sulfur 4, chlorine 3, sodium 2, magnesium 0.7. According to Sherman[141], the percentage composition of the average human body is approximately: nitrogen 3, calcium 2, phosphorus 1, potassium 0.35, sulfur 0.25, sodium 0.15, chlorine 0.15, magnesium 0.05, iron 0.004, manganese 0.0003, copper 0.00015, iodine 0.00004 and other trace elements, including zinc (see Sects. 6.4.2 and 6.6.IV for details). In an average 70-kg (155-lb) body this amounts to about 2.1 kg nitrogen, 1.4 kg calcium, 700 g phosphorus, 245 g potassium, 175 g sulfur, 105 g sodium, 105 g chlorine, 35 g magnesium, 2.8 g iron, 0.21 g manganese, 0.105 g copper, 0.028 g iodine.

From the structural viewpoint, the bony skeleton is composed mostly of calcium and phosphate; 99 per cent of the body calcium and 90 per cent of the phosphorus is in the skeleton. The mineral proportions in bone may be roughly represented by the formula $CaCO_3 \cdot 2$ to $3Ca_3(PO_3)_4$, or more precisely[142] $[Ca_{8.50}Mg_{0.25}Na_{0.19}]\ [(PO_4)_{5.07}(CO_3)_{1.24}](H_2O)$.

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[139] Ashworth, U. S., and Brody, S., "Endogenous nitrogen studies", Univ. Missouri Agr. Exp. Sta. Res. Bulls. 189, 190, 1933; 223, 228, 1935.

[140] Mitchell, H. H., and Carman, G. G., *J. Biol. Chem.*, **60**, 613 (1924); **68**, 183 (1926). Boas-Fixsen, M. A., "The biological value of protein", *Nut. Abstr. Rev.*, **4**, 447 (1935).

[141] Sherman, H. C., "Chemistry of food and nutrition", Macmillan, 1941. Sherman and Lanford, C. S., "Essentials of nutrition", Macmillan, 1940. For specialized monographs, see Shohl, A. T., "Mineral metabolism", Reinhold Pub. Corp., 1939. Wirtshafter, Z. T., "Minerals in nutrition", Reinhold Pub. Corp., 1942. Shils, M. E, and McCollum, E. V., *J. Am. Med. Assn.*, **120**, 609, 1942. Macy, I. G., *Id.*, p. 34.

[142] Hendricks, S. B., and Hill, W. L., *Science*, **96**, 255 (1942).

From the catalytic viewpoint (Sect. 6.4.2), the minerals (including calcium and phosphorus) that function at trace levels serve as prosthetic groups, or coenzymes, or activators, as do vitamins, in electron-transfer enzyme systems. Some of these elements are associated with or constituents of, among others, iron in hemoglobin and cytochrome oxidases; magnesium in chlorophyll, carboxylases, phosphatases; manganese in arginase; copper in hemocyanin and many oxidases; calcium in some oxidases; zinc in carbonic anhydrase, in uricase, as carboxylase activator and possibly as catalyst for insulin storage in the pancreas (milk contains 0.5 mg zinc per liter); aluminum in a succino-oxidase system; and phosphates in phosphorylation. Many other trace elements must have similar functions because they are almost universally present, and their absence is associated with diseases similar to those due to vitamin deficiency. For instance, cobalt is necessary in traces, about 0.05 mg per day for sheep and 1 mg per day for cattle. Like excess copper, excess cobalt is toxic, causing the blood disease polycythemia. Minute traces of boron are essential, at least for plants, and it is universally found in milk and blood. Fluoride seems to be essential in minute traces, especially for healthy teeth; and as for copper, it is very toxic if taken in excess of about 1 mg per liter (1 ppm) water. Traces of arsenic are found in human blood.

As regards iron, 65 per cent of the body iron is in the blood, 30 per cent in the liver, bone marrow and spleen, and 5 per cent in other tissue. Liver is the richest animal dietary source of iron (20 to 80 ppm*) and also of copper (20 ppm). Egg yolk is even richer in iron (85 ppm). While the iron level in milk is low (2.5 ppm iron and 0.2 ppm copper), it is highly available. The blood-regenerating properties of foods and feeds are dependent not only on the content of iron, but also on the degree of its utilization. For instance[143], blood is rich in iron (37 mg per 100 cm blood), but only about 11 per cent of it is utilized; hence only 4 mg iron per 100 g blood is available. Heart muscle is poor in iron (15 mg per 100 g muscle), but as 90 per cent of it is utilized, 14 mg iron per 100 g muscle is available. Similarly, spinach is very rich in iron (38 ppm) but only 20 per cent of it is available; carrot is poor in iron (6 ppm), but 100 per cent of it is available. It thus appears that the available (rather than total) iron is 40 mg for 100 g liver, 15 for heart, 7 for skeletal muscle, and 4 for blood. Blood is richest in iron but poorest as a dietary iron food.

Liver, kidney, and gizzard have the highest overall blood-regenerating values, followed by egg and heart; of plant products, apricots, peaches, prunes, and apples stand high next to the liver-kidney category[144]. Most leafty vegetables are relatively poor iron foods although rich in iron, partly because of its relative unavailability.

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* ppm stands for parts per million, that is mg per kg.

[143] Sherman, W. C., *et al.*, *J. Biol. Chem.*, **107**, 383 (1934); **119**, 725 (1937).

[144] Robscheit-Robbins, F. S., *Physiol. Rev.*, **9**, 666 (1929); *J. Am. Diet. Assn.*, **8**, 387 (1932–33).

There is usually no lack of iron in natural foods, but if the soil is poor in iron, the foods may be likewise. In such cases of nutritional anemia, the diet is supplemented with iron, usually in the form of ferric ammonium citrate for humans and ferrous sulfate ("copperas") for animals[145], about half pound per 100 pounds feed. (The dosage for humans is about 1 g per day of ferrous sulfate or 5 g a day of ferric and ammonium citrate.)

The essential need of copper for iron utilization in hemoglobin building is known[146]. One must be cautious, however, in feeding copper as it is toxic above a certain low level. Young women are said[146a] to need 2.0 to 2.5 mg copper a day, an amount obtained from otherwise mediocre food. There is probably enough "impurity" copper in commercial iron preparations to meet all needs. In the "salt sick" regions of Florida, it is customary to add to 100 lbs common salt for livestock about 25 lbs red oxide of iron, 2 lbs "snow form" copper sulfate, and 1 oz cobalt chloride.

Blood regeneration is also dependent on many other factors, including hormones, of which the antipernicious anemia-factor in liver is one, and on vitamins and trace elements such as cobalt in ruminant iron utilization. Deficiency of cobalt causes "coast disease" in South Australia[147], "enzootic marasmus" in West Australia[148], "bush sickness" in New Zealand[149], "salt sickness", "hill sickness", and just plain sickness in Florida[150], cured by drenching the animals with 1 mg cobalt per day. "Bush sick soils" contain 0.12 per cent cobalt as contrasted to 0.61 per cent in healthy soil[151].

As explained elsewhere (Sects. 20.2 and 21.2), milk is the best, and practically indispensable, source of calcium. Two large glasses a day supply all the needed calcium. In such countries as China where milk is not available, bones are consumed as such and in bone soups cooked in "sweet and sour" (with vinegar). The vinegar disintegrates the hard bone and renders its calcium available. It is customary for dairymen to keep bone meal before their dairy cattle at all times to supply the calcium for milk production. The bone meal is supplemented with other minerals, such as iron, copper, and cobalt, as required to meet the mineral deficiencies in the soil. The bone meal is also often supplemented with vitamin D in one of several forms to facilitate calcium absorption (Sect. 7.5).

When a soil is deficient in minerals, this is reflected in the composition of the plant. For example, in a recent survey, the calcium content in alfalfa ranged from 0.5 to 5.0 per cent, and the iron content in cabbage ranged from 1 to 10 ppm, depending on the soil[152]. The composition of the plants in turn is reflected in the animals which consume them. This is one explanation for the geographical differences in size and vigor of plants and animals[153]. Some authors[154] attribute the increase of many diseases, from hay fever to tooth decay and from sterility to grass tetany (grass tetany may be due, among other factors, to magnesium deficiency[155]), to a decline in soil fertility. However, the minerals of commerce are inexpensive, and it is a simple matter to supplement table salt with the deficient minerals as is done now with iodine. As a result, goiter has been practically abolished. Tooth decay (in children) is greatly reduced by adding to the city water supply one part per million of fluoride[156] (or even by applying 2 per cent NaF solution to the crown surface directly[157]). However, the mineral composition of the soil may influence the organic composition of the plant, for example its protein and vitamin[158] content; a regional agricultural experiment station was recently established in Ithaca, New York, to investigate the nutritional value of plants in relation to the composition of the soil.

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[145] Davison, L. S. P., and Leitch, I., *Nut. Abstr. Rev.*, **3**, 901 (1934).

[146] Ref. 73, Ch. 6.

[146a] Liverton, R. M., and Binkley, E. S., *J. Nut.*, **27**, 43 (1944).

[147] Lines, E. W., and Marston, H. R., *J. Council Sci. & Ind. Research* (*Australia*), **8**, 11, 117 (1935).

[148] Filmer, J. F., *Australian Vet. J.*, **9**, 163 (1933); **10**, 83 (1934).

[149] Wall, E. M., *New Zealand J. Sci. Tech.*, **18**, 642 (1937).

[150] Becker, R. B., Neal, W. M., and Shealy, A. M., Fla. Agr. Exp. Sta. Bull. 231, 1931. Rusoff, L. L., *Id.*, Bull. 356, 1941. Neal and Ahmann, C. F., *J. Dairy Sci.*, **20**, 741 (1937). Killhan, B. J., *Am. Vet. Med. Assn.*, **99**, 279 (1941).

[151] McNaught, K. J., *New Zealand J. Sci. Tech.*, **18**, 655 (1937). Kidson, E. B., *Id.*, p. 694.

To sum up, inorganic elements have important functions in catalytic processes and in structural elements. What was said about the effects of vitamin deficiency is applicable to mineral deficiency also, as minerals are prosthetic groups and coenzymes of various oxidation catalyst systems. The composition of the soil affects that of plants and animals, with consequent influence on human welfare.

In human diet, normally, only two minerals, calcium and iron, are likely to be deficient. The average adult need for calcium is about 0.7 g and for iron 12 mg. The best calcium food is milk, which furnishes about 0.56 g per pint, about ¾ of the day's need, followed by other dairy products—1 oz cheddar cheese furnishes 0.27 g—and by greens, such as turnip greens, mustard greens, collards, each of which furnish about 0.3 g calcium per serving of 100 g or 3½ oz. As previously noted, liver is the best source of iron, about 8 mg per 100-g serving, followed by other visceral organs, and by fruits, as peaches, prunes and apples. A serving of greens, such as turnip tops, beet greens, and chard, each furnishes about 3 mg iron; 100 g (4 slices) whole-wheat bread furnishes 3 mg, but white bread only 0.9 mg iron.

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[152] Cf., Beeson, K. C., "The mineral composition of crops with reference to the soils in which they were grown". U. S. Dept. Agr. Misc. Publ. 369, 1941. Maynard, L. A., *Ann. Rev. Bioc.*, **10**, 449 (1941); *J. Am. Med. Assn.*, **120**, 692 (1942).

[153] Ashton, J., "The influence of geographical conditions on cattle development", Univ. Missouri Agr. Exp. Sta. Res. Bull, 141, 1930.

[154] Albrecht, W. A., *Chem. Eng. News*, **21**, 221 (1943).

[155] Sjollema, B., *Nut. Abstr. Rev.*, **11**, 621 (1930); *Klin Wochschr.*, **11** 989 (1932). Huffman, C. F., Moore, L. A. Duncan, C. W., *et al.*, *J. Biol. Chem.*, **69**, 101 (1926); *Arch. Path.*, **26**, 820 (1938); *J. Dairy Sci.*, **21**, 689 (1938). Schmidt, C. L. A., and Greenberg, D. M., *Physiol. Rev.*, **15**, 297 (1935); *Ann. Rev. Bioc.*, **8**, 269 (1939). McCollum, E. V., *et al.*, *J. Biol. Chem.*, **96**, 519 (1932); **100**, 603 (1933); **106**, 573 (1934); *Am. J. Physiol.*, **101**, 454 (1932); **112**, 356 (1935).

[156] McClure, F. J., *Am. J. Dis. Child.*, **66**, 362 (1943).

[157] Knutson, J. W., *Public Health Repts.*, **58**, 170 (1943).

[158] Nelson, D., *et al.*, *Proc. Soc. Exp. Biol. Med.*, **52**, 1 (1943).

The following salt mixtures fed to rodents in synthetic diets at 4 per cent level of the air-dry food may indicate what is thought by some to furnish adequate mineral nutrition.

Hamilton and Hogan[159] (Hamsters)	
$Ca_3(PO_4)_2$	376
KH_2PO_4	212
$CaCO_3$	125
KCl	112
NaCl	69
$MgSO_4 \cdot 7H_2O$	33
$MgCO_3$	25
$MnSO_4 \cdot 4H_2O$	26
$FePO_4 \cdot 4H_2O$	21
$CuSO_4 \cdot 5H_2O$	1.4
$Al_2(SO_4)_3 \cdot K_2SO_4 \cdot 4H_2O$	0.17
KI	0.08

Sure[160] (Rats)	
K_2HPO_4 (anh.)	645
$CaCO_3$	600
NaCl	335
$CaHPO_4 \cdot 2H_2O$	190
$MgSO_4$ (anh.)	99
Ferric citrate (pow'd)	55
KI	1.6
$ZnCl_2$	0.5
NaI	0.5
$CaCl_2$	0.5
$Na_2B_4O_7$ (anh.)	0.5
$CuSO_4$ (anh.)	0.4
$Al_2(SO_4)_2 \cdot K_2SO_4$	0.4

20.9. Note on energy relations in nutrition. Table 20.1 indicates the human dietary need for energy. Roughly speaking, a 70-kg mature person at rest requires about 30 Calories per kg body weight; at light work 40 Calories per kg; at moderate work 50 Calories per kg; at hard work 60 Calories per kg. Larger individuals require less energy per unit weight (Ch. 15).

A 100 g or 3½ oz serving of bread (4 slices) furnishes 250 to 300 Calories, meat 150 to 400 Calories (depending on fat content, ham is 500 Calories, lean beef heart 150 Calories, good beef loin 375 Calories). In terms of Calories per pound for broad categories, meats, fish, and poultry have a value of about 1100 Calories per pound; fresh eggs 635; milk 360; butter 3320, other fats 3900; potatoes 330, fresh and canned fruits (other than citrus) 290, dried fruits 1280.

As explained in Ch. 6 and Sects. 20.2 to 20.5, the degree of utilization of the energy depends on the balance between the nutrients and the level of dietary energy intake (Ch. 5) in relation to need; hence the given energy values of foods have such values only under certain conditions.

20.10. Summary and appendix. This chapter discusses selected topics in nutrition germane to the spirit of this book, including the following.

(1) Species differ in dietary dependence on vitamins and amino acids. Ruminants, such as cattle and sheep, are unique in not being dependent on dietary water-soluble vitamins; indeed, vitamin A (carotene) is the only one which often becomes limiting in this class of animals, especially as much of the carotene is destroyed in the rumen. Ruminants are also unique in being able to convert dietary non-amino nitrogen into amino acids and proteins. These peculiarities and their ability to consume roughage which cannot otherwise be utilized in the agricultural economy, and to convert

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[159] Hamilton, J. W., and Hogan, A. G., *J. Nut.*, 27, 213 (1944).

[160] Sure, B., *Id.*, 26, 276 (1943).

it very efficiently into milk and (much less efficiently) meat, places the ruminant, especially the highly developed dairy cow, in a class by itself as a converter of feed into food. The simpler the alimentary canal, and the less the ability to handle bulky roughage, the greater the possibilities of developing dietary deficiencies.

(2) Species and individuals differ in "nutritional wisdom", in the spontaneous selection of foods that promote well being. In man, the "spontaneous" choice is perhaps modified by intelligence which is, however, confused by social conditioning factors. This confusion is, on the other hand, ameliorated by rapid accumulation of knowledge as to what constitutes an optimal diet, which is discussed at some length.

(3) Several methods are used for comparing the nutritional values of food combinations, among which the *ad libitum* and paired-feeding methods are discussed in detail, and briefer attention is given to the total life-history method.

(4) The nutrients are grouped into nitrogenous, energy-yielding, vitamin, and mineral. Foods and feeds vary in nutritional value because of differences in digestibility and difference in balance between nutrients, not only between these four categories of nutrients but also between the constituents, individual amino acids, vitamins, and minerals. The balance between the nutrients is not at a sharp point but in a broad zone, and wise dietary economics depend on the appreciation of the degree of freedom of movement within this zone.

(5) With the exception of vitamin A, which all species need, there are enormous species differences in reaction to a given vitamin deficiency, even if ruminants are omitted from consideration.

(6) Minerals, such as calcium and phosphorus compounds, function as structural elements; but these two, as well as all the essential trace elements, also act as catalysts in oxidation processes in the manner of vitamins. The lack of traces of cobalt in the soil, for example, was the limiting factor in the progress of the dairy and sheep industries in Australia and Florida; the discovery of the indispensable nature of cobalt changed the outlook for these industries and enlarged the perspective of the science of nutrition, substantiating the importance of "little things" in nutrition.

This chapter touched briefly on a few selected nutritional topics; it could be greatly expanded. The science of nutrition, as contrasted to the arts and instinct of feeding, is very new, very fertile, and is expanding very rapidly. The field of nutrition includes the identification of nutrients required by different species; their minimal and optimal consumption in relation to age (Ch. 14), to body size (Ch. 15), to climate (Ch. 11), to various functions (growth, reproduction, lactation, muscular work, fattening, and so on); nature of the participation and mechanism of action of each nutrient, especially of the catalysts (Ch. 6); consequence of dietary deficiencies and excesses (Chs. 5 and 18); nutrient balance (antagonisms and synergisms) and replacement; composition of foods with respect to nutrients and to other factors, such as bulk of a certain character and related factors in intestinal hygiene; influence of food processing (heating, milling, etc.) and of environmental factors (soil, temperature, light) on composition and nutritive value; neuro-psychic drives for each of the foods and the effects of various nutrient proportions in the diet on the neuro-psychic behavior, including nervous stability and mental activity, and so on. All these factors enter into the overall and long-range efficiency complex discussed in this book.

The following appendix presents data in tabular form for recommended nutrient allowances for man (Table 20.1); actual food consumption (Table 20.1a); composition of foods, presented in various forms (Table 20.1d); efficiency and economy with which various classes of food are produced (Table 20.2a and b).

Table 20.1. Recommended Dietary Allowances.
National Research Council, Circular 115, 1943

	Calories	Protein (g)	Calcium (g)	Iron (mg)	Vitamin A (I.U.)	Thiamin (B_1) (mg)	Riboflavin (mg)	Niacin (Nicotinic Acid) (mg)	Ascorbic Acid (mg)	Vitamin D (I.U.)
Man (70 Kg.)										
Sedentary	2500	70	0.8	12	5000	1.5	2.2	15	75	
Moderately active	3000	—	—	—	—	1.8	2.7	18	—	
Very active	4500	—	—	—	—	2.3	3.3	23	—	
Woman (56 Kg.)										
Sedentary	2100	60	0.8	12	5000	1.2	1.8	12	70	
Moderately active	2500	—	—	—	—	1.5	2.2	15	—	
Very active	3000	—	—	—	—	1.8	2.7	18	—	
Pregnancy (latter half)	2500	85	1.5	15	6000	1.8	2.5	18	100	400–800
Lactation	3000	100	2.0	15	8000	2.3	3.0	23	150	400–800
Children up to 12 years:										
Under 1 year	100/Kg.	3–4/Kg.	1.0	6	1500	0.4	0.6	4	30	400–800
1–3 years	1200	40	1.0	7	2000	0.6	0.9	6	35	
4–6 years	1600	50	1.0	8	2500	0.8	1.2	8	50	
7–9 years	2000	60	1.0	10	3500	1.0	1.5	10	60	
10–12 years	2500	70	1.2	12	4500	1.2	1.8	12	75	
Children over 12 years:										
Girls, 13–15 years	2800	80	1.3	15	5000	1.4	2.0	14	80	
16–20 years	2400	75	1.0	15	5000	1.2	1.8	12	80	
Boys, 13–15 years	3200	85	1.4	15	5000	1.6	2.4	16	90	
16–20 years	3800	100	1.4	15	6000	2.0	3.0	20	100	

The vitamin D requirements of adults are not known, but they are probably the same as for children. The copper requirement is approximately one tenth that of iron. The iodine requirement is probably 0.002 to 0.004 mg/kg body/day; magnesium perhaps 12 mg/kg/day; manganese perhaps 0.25 mg/kg/day.

Table 20.1a. Prescribed and Consumed Food in the United States Army. (Average of 117 surveys, 1941–42 by Col. P. E. Howe[1])

Food, lbs/man/day				Nutrients/man/day			
	issued	consumed	% wasted		issued	consumed	% of total Cal.
Milk and milk products	1.030	0.974	2.5	Total Calories	4100	3888	
Meats	0.940	.935	12.2	Protein (g)	130	124	
Eggs	.150	.145	6.0	(Cal)	520	500	13
Butter	.088	.091	1.3	Fat (g)	193	193	
Other fats	.073	.075	6.6	(Cal.)	1737	1737	44
Grain products	.651	.578	9.3	Carbohydrate (g)	460	415	
Legumes	.052	.057	8.7	(Cal)	1840	1660	4
Sugar and sirups	.261	.263	7.0	Calcium (mg)	954	883	
Leafy vegetables	.387	.314	20.9	Phosphorus (mg)	1946	1882	
Tomatoes	.137	.133	5.2	Iron (mg)	28	25	
Citrus fruits	.205	.229	6.3	Vitamin A (I.U.)	10760	9255	
Potatoes	.769	.650	16.5	Thiamine (mg)	2.2	2.1	
Other vegetables	.278	.212	14.6	Riboflavin (mg)	3.0	2.3	
Other fresh fruits	.348	.365	8.9	Nicotinic acid (mg)	32.0	27.4	
Dried fruits	.063	.017		Ascorbic acid (mg)	93.2	86.0	

[1] Cf., *Ann. Am. Acad. Pol. Soc. Sci.*, **225**, 78 (1943).

According to H. K. Stiebeling [*Fed. Proc.*, **1**, 328 (1942)], the average per capita daily food consumption (lbs) of civilians in 1936 was milk 1.03, meat, poultry and fish 0.326, eggs 0.090, butter and other fats 0.159, grain products 0.570, legumes and nuts 0.036, sugar and sirup 0.208, leafy vegetables 0.230, tomatoes and citrus fruits 0.222, potatoes 0.405, other vegetables and fruits 0.529.

Table 20.1b. Nutrients per Pound of Food Groups "as Purchased" (Based on Food Prescribed for U. S. Army, May–October, 1941). G. H. Berryman and P. E. Howe, *J. Nut.*, **27**, 237 (1944).

Group	Calories	Protein (g)	Fat (g)	C(OH) (g)	Ca (mg)	P (mg)	Fe (mg)	Vitamin A (I.U.)	Thiamine (mg)	Riboflavin (mg)	Niacin (mg)	Ascorbic acid (mg)
Meats, fish and poultry	1120	65	95	2	41	719	9.8	120[1]	1.87[2]	.77[1]	19.4	3
Eggs, fresh	635	52	46	3	218	848	10.9	4040	.56	1.45	.2	0
Milk products (equivs.)	360	16	21	25	556	427	.9	1020	.11	.74	.4	4
Fats, butter	3320	3	367	2	73	73	.9	14970	.01	.04	.5	0
Fats, other	3900	1	432	3	2	9	.1	120	.01	.01	.2	0
Grain products[3]	1360	40	14	270	160	482	9.0	20	1.12	.83	11.2	0
Legumes, dry and nuts	1630	97	15	276	538	1968	40.7	10	2.40	1.33	12.5	0
Sugars and syrups	1680	1	0	420	37	16	2.2	0	.00	.00	.0	0
Vegetables, leafy green and yellow	150	7	1	30	145	152	3.5	14750	.29	.24	.27	91
Tomatoes	130	5	1	26	61	160	2.6	3860	.36	.20	2.2	78
Citrus fruits	140	2	1	32	91	66	1.2	90	.23	.07	1.5	118
Potatoes, white	330	8	0	73	30	186	2.8	150	.34	.19	4.5	46
Vegetables, other	180	6	1	37	102	173	1.9	180	.12	.22	.9	49
Fruits, other than citrus fresh and canned	290	2	1	69	34	51	1.3	1940	.09	.17	1.4	24
Fruits, dried	1280	12	2	302	245	452	18.0	8320	.47	.60	6.6	0

[1] When liver is used add 25,000 I.U. Vitamin A and 14.6 mg. of riboflavin per pound of liver.

[2] Use this figure only when the combined weight of the lean pork cuts (viz., fresh and cured ham, pork loin and chops, Boston butt, and shoulder) is 15% or more of the weight of the meat group. When the combined weight is less than 15%, compute the thiamine thus: (wt. in lbs, of lean pork cuts × 5.9) plus (wt in lbs, of all other meat × 1.0). This gives the quantity of thiamin in milligrams in the entire group.

[3] Values based on new enrichment levels effective October 1, 1943. When enriched flour and bread are not used, count thiamine in the entire group as only 0.59 mg per pound, riboflavin 0.29 mg per pound, nicotinic acid 4.2 mg per pound, and iron 5.5 mg per pound (based on "straight" flour); no changes need be made in other nutrients.

Table 20.1c. The monetary cost of nutrients per day of several foods.

The first column under each nutrient gives the cost in cents for the day's recommended allowance for the average adult, not counting the value of other nutrients in the food (as cost of 70 gm protein recommended for the average 70-kg man, not counting other nutrients in the food); the second column indicates the percentage of the daily requirement supplied by a serving (weights which are given in the second column from the left). Thus 244 gm (or 8.6 oz or ½ pint) milk supplies 40% of the daily calcium requirements, 12% of the protein requirement, 20% of the riboflavin requirement, and so on. Modified from Barbara Kennedy, Cornell Univ. Agr. Exp. Sta. Bull, 774, 1941.

Food	Weight per serving "as purchased," g	Retail price cents/lb	Protein		Calcium		Iron		Vitamin A		Thiamine		Riboflavin		Ascorbic acid	
			Cost (cents) for 70 g (day's need)	Per cent of day's need in a serving	Cost (cents) for 0.8 g (day's need)	Per cent of day's need in a serving	Cost (cents) for 12 mg (day's need)	Per cent of day's need in a serving	Cost (cents) for 5000 I.U. (day's need)	Per cent of day's need in a serving	Cost (cents) for 1.8 mg (day's need)	Per cent of day's need in a serving	Cost (cents) for 2.7 mg (day's need)	Per cent of day's need in a serving	Cost (cents) for 75 mg (day's need)	Per cent of day's need in a serving
Apples	170	5.4	276	.7	159	1.3	47	4	105	2	63	3	142	1.5	24	9
Bananas	156	6.3	115	1.9	210	1	43	5	36	6	86	3	64	4	16	13
Beans, green	100	11.3	82	3.3	39	7	27	10	13	20	64	4	60	5	13	20
Beans, navy, dry	28	7.1	5	9	8½	5	2	24	—	—	6	8	—	—	—	—
Butter	13	37	—	—	400	0.3	—	+	17	6	—	—	—	—	—	—
Bread, white (4 slices)	100	8.3	14	14.4	23	9	27	7	—	—	55	3	—	—	—	—
Bread, 100% wheat (4 slices)	100	9.4	13	17	23	10	15	16	—	—	12	19	62	3	—	—
Cabbage	75	3.7	42	1.7	17	4	29	3	49	2	23	3	29	3	1	60
Cheese, American	23	27	14	10	5	27	55	3	15	9	237	0.6	21	7	—	—
Cornflakes	28	15	28	3.3	177	0.5	15	6	—	—	—	—	—	—	—	—
Eggs	50	35/doz	31	9.6	76	4	24	12	29	10	71	4	48	6	—	—
Liver	100	25	21	29	442	1.4	9	68	3	180	48	13	9	67	12	50
Milk, whole (½ pt, 8.6 oz)	244	13/qt	27	12	8½	40	75	4	56	6	—	—	15	20	75	5
Molasses	35	13	80	1.2	8½	11	5	22	—	—	38	9	—	—	—	—
Orange (medium)	150	31	134	1.9	53	5	41	6	200	2	40	7	310	1	2	120
Peaches, canned	100	18 (#2½ can)	204	1.1	194	1.1	131	2	14	16	169	1	127	2	41	5
Peas, canned	100	15 (#2 can)	53	5	152	1.8	29	9	13	21	13	20	73	4	20	13
Potatoes	120	2.6	23	3.8	47	2	10	9	119	1	11	8	43	2	4	20
Pork chops	100	32	31	29	780	1.1	71	12	—	—	13	66	106	8	—	—
Prunes, dried	39	10	84	1	35	2.4	10	8	5	16	30	3	—	—	—	—
Rolled oats	25	7.3	7	6	20	2	4	10	—	—	5	8	41	1	—	—
Round steak	100	36	28	30	525	1.6	35	30	857	1	129	7	103	8	—	—
Salmon, red, canned	100	25	20	28	67	8	51	10	85	6	—	—	67	8	—	—
Spinach	100	7	68	3	—	—	9	21	½	500	30	7	15	14	2	100
Sweet potato	150	4.5	45	4	47	4	18	10	2	100	23	8	35	5	4	40
Tomato, canned	100	9 (#2 can)	97	1.7	132	1.3	50	3	8	20	40	4	75	2	6	30

Table 20.1d. Nutrients per 100 Grams Edible Food[1]

Food	Calories	Protein (g)	Carbohydrate (g)	Fat (g)	Calcium (mg)	Phosphorus (mg)	Iron (mg)	Vitamin A (I.U.)	Thiamine (mcg)	Riboflavin (mcg)	Niacin (mg)	Water (g)
Bread, whole wheat	260	9	50	3.5	50	185	3	15	300	150	2	36
Bread, white	260	9	50	2.0	25	100	0.9	0	50	10	1	36
Wheat, whole	360	12	75	2.0	53	375	4.0	20	500	85	7	11
Wheat, white flour	350	11	75	0.9	16	100	1.0	0	50	15	1	12
Wheat, germ	380	25	49	10	70	1000	9.0	100	2000	700	6	11
Wheat, bran	360	16	66	4	120	1200	13	140	520	350	30	7
Rolled oats	400	14	68	7.5	70	390	4	0	800	140	1.3	8
Corn, whole	360	9	72	4	17	190	0.9	600	200	120	2	10
Rice, unpolished	355	7.5	77	1.7	90	300	2	0	300	150	7	12
Rice, polished	350	7.5	79	0.3	9	100	0.9	0	30	50	1	12
Soybean flour[5]	380	37	10	20	200	450	7	—	—	—	—	7
Peanut butter	610	26	26	48	70	400	2	360	600	500	15	2
Yeast, dry brewers[2]	350	46	37	1.6	77	190	5	0	14000	5000	50	7
Dehydrated cereal grass, age 30 days[3]	—	25	—	7	—	—	—	960000[3]	12800	2620	8	—

(Continued)

Table 20.1d (Continued)

Food	Calories	Protein (g)	Carbohydrate (g)	Fat (g)	Calcium (mg)	Phosphorus (mg)	Iron (mg)	Vitamin A (I.U.)	Thiamine (mcg)	Riboflavin (mcg)	Niacin (mg)	Water (g)
Skimmilk powder[4]	360	36.9	50.3	0.9	1310	1020	--	150	355	2100	1	3.3
Wholemilk powder	500	26	38	27	920	—	1.5	1600	315	1600	1	2.5
Skimmilk, fresh	36	3.5	5.0	0.2	120	96	0.2	15	30	170	0.11	90.5
Wholemilk, fresh	68	3.5	4.9	3.9	116	93	0.2	200	30	170	0.11	87
Cheese, cheddar	400	24	1.7	32	920	680	1.4	2000	40	450	—	39
Cheese, cottage	100	20	4	0.5	80	300	0.1	25	30	(composition depends on fat)		74
Egg, fresh	158	12.8	0.7	11.5	65	180	3	1000	150	300	7	74
Beef, liver	130	20	2	6	10	400	8	9000	300	2500	20	70
Beef steak	200	19	0.5	12	10	200	3	20	200	300	5	0-70
Chicken	130	20	0	12	10	220	3	—	120	175	7	565
Herring	140	19	0	6.7	20	220	0.6	200	120	1000	4	73
Salmon	220	17	0	16.5	25	250	1.2	250	120	220	7	63
Cabbage	25	1.4	4.3	0.2	45	29	.5	40	80	65	21	92
Lettuce	16	1.2	2.3	0.2	45	40	.7	200	90	100	21	95
Apples	60	0.3	14	0.4	7	12	0.4	50	45	75	21	84

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[1] Chatfield, C. and Adams, G., "Proximate Composition of American Food Materials". U.S.D. Agr. Circ. 549, 1940. Daniel, E. P., and Munsell, H. E., "Vitamin Content of Food", Id., Misc. Pub. 275, 1937. Booher, L. E., *et al.*, "Vitamin Values of Foods", Id., Circ. 638, 1942. Hewston, E. M., and Marsh, R. L., "Vitamin Values of Foods", Id., Misc. Pub. 505, 1942. Munsell, H. E., "The Vitamin A, Vitamin B, Vitamin C, and Riboflavin Content of Common Foods", *Milbank Memorial Fund Quarterly*, **21**, 102 (1943). Current (1943-44) issues of the *Journal American Dietetic Association*. Fixsen, M. A. B., "Vitamins in Human Foods", *Nut. Abst. Rev.*, **7**, 8, 23, (1937-38); **8**, 281 (1938-39); **9**, 295 (1939-40).

[2] Standard Brands Circular (1944) cites the following values per 100 gm of its dry brewers yeast: water 4.1 g, protein 50 g; carbohydrate 33 g; fat 5.8 g; Ca 70 mg; P 161 mg; Fe 17 mg; Cu 2.1 mg; Zn 12.5 mg; Mg 270 mg; thiamine 50000 to 60000 mcg; riboflavin 7000 mcg; nicotinic acid 50 to 70 mg; pyridoxin 2.5 to 5 mg; pantothenic acid 10 to 60 mg.

[3] Kohler, see next table. The values are on moisture-free basis.

[4] O'Malley, C. M., and Gross, A. M., Am. Dry Milk Institute, Letter Nov. 1943. Also ash 8.16% as contrasted to 5.85% in whole dry milk.

[5] Burkholder, P. R., [*Science*, **98**, 188 (1943)] cites the following vitamin values for edible varieties of mature soybeans, mcg/gm dry matter: thiamine 9.0, riboflavin 2.3, niacin 20, pyridoxine 6.4, biotin 0.61, pantothen 12; for green or immature soybean, thiamine 6.4, riboflavin 3.5, niacin 40, pyridoxine 3.5, biotin 0.54, pantothen 12, ascorbic acid 0.21 mg/gm dry matter.

Table 20.1e. Composition of Dehydrated (at 80°C) Young (3-6 Weeks after Planting) Cereal Grass on Moisture-Free Basis

Data kindly furnished by George O. Kohler through courtesy of W. R. Graham, Jr., Basis of charts 2 and 3; *J. Biol. Chem.*, **152**, 215 (1944).

Age from planting (days[1])	Vitamin B_1 (thiamine) (mcg/g)	Vitamin B_2 (riboflavin) (mcg/g)	Vitamin C (ascorbic acid) (mg/g)	Carotene[3] (mg/g)	Biotin (mcg/g)	Pantothenic Acid (mcg/g)	Niacin (mcg/g)	*l. casei* growth factor[2] (mcg/g)	Protein (per cent)	Fat (pet. ether extract) (per cent)	Fiber (per cent)	Chlorophyll total (mg/g)	Solids in fresh grass (per cent)
24	12.9	26.8	6.41	0.549	.181	13.7	92.5	17.0	25.1	7.2	16.1	8.35	11.0
27	12.9	26.5	6.88	0.540	.185	14.6	81.5	18.1	25.8	8.7	17.2	7.83	17.0
30	12.8	26.2	6.11	0.579	.220	17.0	77.7	14.6	24.0	8.3	18.3	8.36	19.0
33	9.4	23.4	4.28	0.479	.239	17.7	69.7	12.3	21.8	7.2	20.4	7.10	15.0
36	10.9	22.8	4.97	0.505	.204	17.4	64.9	9.4	21.3	6.3	22.3	7.53	14.0
39	8.5	20.0	3.24	0.411	.231	16.5	58.6	10.7	18.2	7.0	23.8	6.18	15.0
42	2.1	15.7	3.10	0.348	.152	13.0	53.1	7.7	19.7	6.7	28.9	4.83	15.0
45	6.5	14.6	3.69	0.344	.173	16.8	52.9	6.4	16.3	6.8	25.7	5.16	16.0

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[1] The vitamin, protein, and fat content of the leaves is near maximum at the jointing stage. Most of Dr. Kohler's plants jointed by the 27th day (about 13½ inches long). The first grain heads appeared on the 39th day. The *l. casei* growth factor data are not claimed to be (by Dr. Graham) "as absolutely sound".

[2] *l. casei* growth factor, or "Norit eluate factor", is presumably identical with folic acid, vitamin B_c (Hogan's anti-anemia vitamin).

[3] The carotene values appear high, but not unreasonable. Thus Vernon Booth (*Chemistry and Industry*, **61**, 255, 1942) quotes in mg per 100 gm fresh mixed grasses in June, carotene 6.0, thiamine 0.11, riboflavin 0.13, nicotinic acid 0.7, ascorbic acid 100. L. A. Moore and R. Ely (*Industrial and Engineering Chemistry*, **13**, 600, 1941) quotes mcg *carotene* per gram *fresh* green material, June grass 155, clover 200, alfalfa leaf 100, carrot root 105. But for hay, alfalfa 2 to 25, soybean 50 to 80; for dehydrated alfalfa leaf about 60.

Table 20.2a. Relative Efficiency of Production of Human Food Nutrients from Livestock

Christensen, R. P., "Using resources to meet food needs," U. S. Dept. Agr., Bur. Agr. Econ., 1943

	Calories (1000's)	Protein (lb)	Calcium (g)	Phosphorus (g)	Iron (mg)	Vitamin A (1000 I.U.)	Thiamine (mg)	Riboflavin (mg)	Niacin (mg)
Yield of nutrients per acre:									
Whole milk	352	39	603	475	1028	991	149	894	508
All dairy products	290	25	385	291	659	933	87	527	289
Dairy enterprise	235	22	277	227	730	669	78	398	991
Eggs	144	26	49	193	2473	916	188	458	57
Chickens	108	25	9	122	1065	—	53	28	3755
Broilers	117	27	10	131	1146	—	57	30	4041
Chicken enterprise	132	26	35	169	1989	599	141	309	1345
Hogs (pork and lard)	500	18	5	100	1411	—	959	130	4974
Steers	57	8	2	40	556	—	34	47	1766
Lambs	115	13	4	81	1102	—	183	124	1853
Yield of nutrients per 100 man-hours of farm labor:									
Whole milk	791	89	1354	1066	2309	2226	335	2008	1141
All dairy products	651	55	864	654	1479	2096	195	1183	649
Dairy enterprise	633	60	746	613	1968	1804	209	1074	2672
Eggs	313	56	108	419	5378	1993	408	996	125
Chickens	322	74	27	363	3166	—	158	83	11160
Broilers	279	64	23	314	2739	—	137	72	9655
Chicken enterprise	317	61	85	405	4775	1438	339	742	3240
Hogs (pork and lard)	1618	58	17	324	4564	—	3102	419	16092
Steers	289	42	11	203	2829	—	171	239	8984
Lamb	521	58	20	364	4981	—	827	563	8377
Yield of nutrients per 1,000 feed units:									
Whole milk	276	31	472	372	805	776	117	700	398
All dairy products	227	19	292	228	515	731	68	412	226
Dairy enterprise	182	17	207	175	565	517	60	308	767
Eggs	113	20	39	150	1931	716	146	358	45
Chickens	83	19	7	94	818	—	41	21	2884
Broilers	98	23	8	110	963	—	48	25	3393
Chicken enterprise	102	20	27	130	1540	464	109	240	1041
Hogs (pork and lard)	349	13	4	70	985	—	670	91	3474
Steers	40	6	2	28	387	—	23	33	1230
Lambs	85	9	3	60	816	—	135	92	1372

Table 20.2b. Relative Efficiency of Production of Human Food Nutrients from Crops

Christensen, R. P., "Using resources to meet food needs," U. S. Dept. Agr., Bur. Agr. Econ., 1943

	Calories (1000's)	Protein (lb)	Calcium (g)	Phosphorus (g)	Iron (g)	Vitamin A (1000 I.U.)	Thiamine (mg)	Vitamin C (g)	Riboflavin (mg)	Niacin (mg)
Yield of nutrients per acre:										
Wheat, whole flour	1,132	90	167	1,177	15,743	—	1,582	0	486	15,274
Wheat, white flour	833	56	35	237	2,351	0	155	0	103	2,329
Corn meal (yellow)	1,122	57	31	441	2,997	347	725	0	94	1,878
Cornflakes	595	29	25	185	4,466	0	0	0	0	837
Oats, rolled	987	78	202	910	12,961	0	2,018	0	374	2,499
Potatoes	2,283	118	348	1,300	19,656	1,074	2,412	265	1,331	31,374
Sweet potatoes	1,801	55	502	649	11,047	55,480	1,409	359	971	16,571
Sugar	6,634	0	0	0	0	0	0	0	0	0
Beans, dry	1,081	150	457	1,430	31,819	0	1,608	0	964	8,653
Peas, dry	1,248	190	257	1,399	21,150	932	4,440	0	1,236	6,343
Soybeans, whole	1,545	339	1,001	2,586	37,033	573	5,152	0	1,323	10,692
Soybeans (oil)	612	0	0	0	0	0	0	0	0	0
Cabbage	870	96	1,459	998	16,128	5,094	2,522	1,741	1,562	9,088
Carrots	2,685	166	2,381	2,291	48,330	431,354	3,652	430	4,278	88,963
Tomatoes	408	41	198	490	10,960	23,588	1,446	455	816	10,552
Apples	1,073	13	98	166	5,080	1,317	415	68	1,166	8,204
Peaches	939	18	150	397	10,483	31,271	369	150	1,106	17,568
Oranges	1,909	68	1,264	901	13,173	2,446	3,818	1,694	1,169	19,088

Table 20.2b (Continued)

	Calories (1000's)	Protein (lb)	Calcium (g)	Phosphorus (g)	Iron (g)	Vitamin A (1000 I.U.)	Thiamine (mg)	Vitamin C (g)	Riboflavin (mg)	Niacin (mg)
Yield of nutrients per 100 man hrs. of farm labor:										
Wheat, whole flour	12,582	1,002	1,852	13,078	174,930	--	17,584	0	5,398	169,722
Wheat, white flour	9,251	621	389	2,629	26,124	0	1,720	0	1,149	25,876
Corn meal (yellow)	4,109	211	114	1,614	10,977	1,272	2,655	0	346	6,879
Cornflakes	2,178	105	93	677	16,359	0	0	0	0	3,065
Oats, rolled	10,963	868	2,245	10,107	144,008	0	22,425	0	4,153	27,761
Potatoes	3,358	174	511	1,912	28,907	1,579	3,547	389	1,957	46,140
Sweet potatoes	1,583	48	440	569	9,691	48,670	1,236	315	852	14,537
Sugar	2,787	0	0	0	0	0	0	0	0	0
Beans, dry	4,159	576	1,756	5,501	122,384	0	6,183	0	3,706	33,283
Soybeans, whole	12,879	2,821	8,343	21,546	308,610	4,779	42,930	0	11,025	89,100
Soybeans (oil)	5,103	0	0	0	0	0	0	0	0	0
Cabbage	799	88	1,339	916	14,796	4,674	2,313	1,597	1,433	8,338
Carrots	829	51	735	707	14,918	133,141	1,127	133	1,320	27,459
Tomatoes	242	24	117	290	6,486	13,959	856	269	483	6,244
Apples	873	10	80	135	4,131	1,071	337	55	948	6,744
Peaches	751	14	120	318	8,387	25,017	295	120	885	14,054
Oranges	1,224	44	810	577	8,445	1,568	2,447	1,086	750	12,236

Table 20.3A. Per Capita Food Consumption in terms of retail purchase weight in pounds per year.*

	1921–26	1926–31	1931–36	1936–41
All foods	1355	1375	1335	1411
Fluid milk, cream	331	341	336	343
Cheese, evaporated milk, ice cream	23	25	26	34
Butter	17.9	17.7	17.7	17.0
Meats, poultry, fish	140	132	131	137
Beef	52	44	46	{56
Veal	7.6	6.1	7.1	
Pork, lean	46	46	41	43
Lamb, mutton	5.2	5.9	6.7	6.7
Chicken	14.8	15.5	14.6	14.7
Eggs (1 doz. = 24 oz)	39.5	40.9	35.5	37.7
Lard	13.5	13.0	12.4	12.7
Bacon, salt pork	20.2	20.1	18.0	18.7
Lard compounds, margarine, mayonnaise, salad oil	9.9	12.4	14.4	17.0
Cereals, flour	227	223	200	196
Potatoes (Irish, sweet)	164	157	157	147
Sugar, sirup	116	102	95	100
Dry legumes, nuts	12	14	15	16
Tomatoes, citrus fruits	48	53	60	84
Leafy, green, yellow vegetables	57	65	67	79
Other vegetables	40	45	45	53
Deciduous fruits	156	163	150	165
Coffee, tea, spices, chocolate	17	17	18	21

* Compiled from *Agricultural Statistics*, U.S.D.A., 1942.

Table 20.3b. Consumption, pounds per capita per year, in the U. S. A.

	1925	1930	1936	1940	1941
Meat and lard:					
Beef	60.0	48.9	57.9	55.1	61.5
Veal	8.6	6.4	8.4	7.4	7.7
Lamb and mutton	5.3	6.7	6.6	6.6	6.9
Pork (excl. lard)	67.3	67.0	55.0	72.9	68.9
Total meats	141.2	129.0	127.9	142.0	145.0
Lard	12.5	12.7	11.3	15.0	14.8
Dairy products, commercial (cities and villages):					
All dairy products, milk equivalents	801	818	797	825	814
Fluid whole milk	353	353	338	347	347
Skimmilk and its products		425	429	450	457
Butter	18.0	17.3	16.5	17.0	16.4
Cheese (except cottage, pot, baker's)	4.6	4.6	5.4	6.0	6.0
Evaporated whole milk	9.2	11.3	14.1	17.5	18.5
Condensed whole milk	1.1	0.8	0.4	0.2	0.2
Ice cream	10	10	10	12	14.5
1 gal. milk = 8.6 lb; 1 qt. milk = 2.15 lb. 1 gal. ice cream = 5 lb.					
Poultry and eggs:					
Chicken	19.8	21.6	19.0	18.9	20.3
Turkey		1.8	2.7	3.6	3.6
Eggs (number, not lb.)	318	331	289	319	316
Oleomargarine	2.0	2.6	3.1	2.4	2.7

Chapter 21

Milk: Nutritional, Social, and Physiological Aspects

Thou shalt have milk for thy food, for the food of thy household, and for the food of thy maidens. *King Solomon*

Milk is the nearest thing we possess to a perfect and complete food, and no other single food can be employed as a substitute. *Hariette Chick*

The production of milk constitutes the most economic method of converting feeding stuffs into animal products and the maintenance of milk supply is the most important object of war-time husbandry. *Norman C. Wright*

21.1: Introduction. The milk problem has surprisingly complex interrelations: energetic efficiency (Chs. 1, 2, 3, 21, 22), endocrinologic (Ch. 7), seasonal (Ch. 8), temperature (Ch. 11), nutritional and medical (Chs. 4, 5, 6, 20, 21, 22), time relations and aging (Chs. 16, 18, 19), evolutionary, organismic and homeostatic (Chs. 7 and 10), form-function (Ch. 17), soil fertility and national stability (Ch. 25), and so on.

Milk production has been said to be the backbone of American agriculture and milk consumption the keystone of American nutrition. The proverbial vigor of the pastoral peoples is undoubtedly associated with their high milk consumption, and Americans match them in vigor.

There is one milking cow for five persons in the U. S. A. At the current rate of milk production (5000 lbs milk per cow per year), one quart is produced per capita per day. Of this one quart about half is consumed in fluid form; the remainder is used for producing butter (about 20 lbs of 4 per cent fat milk for one pound of butter), cheese (about 10 lbs milk per lb cheese), ice cream (over two quarts of milk for one quart of ice cream), evaporated and condensed milk (2.2 lbs milk per lb evaporated milk), powdered milk (8 lbs milk per lb powdered milk), malted milk (2.6 lbs milk per lb malted milk), and so on. The by-products from the production of butter ("defatted milk" or skim milk), cheese (whey), and so on, are utilized as food for man, feed for animals and for the manufacture of various products, such as casein, lactose, confections, vinegar, sizing, various plastics for buttons, "wool", etc.

The importance of milk is indicated by the fact that about one-fifth of the average farmer's cash income is derived from the sale of milk and one-fifth of the average consumer's food dollar is expended for milk and dairy products. (The 1941 American per capita consumption was 164 quarts fluid milk, 18 lbs butter, 6 lbs cheese, 16 lbs evaporated milk, 2 gals ice cream, and considerable amounts of powdered milk). While the dairy industry is gigantic in the aggregate[1], the average dairy farm is small, typically a single-family enterprise. Half the country's dairy cows are in herds of 8 cows or less, and three-fourths are in herds of 15 or less (only 5 per cent of the cows are in herds of 30 to 50 cows, 2 per cent in herds of 50 to 75, and 1 per cent in herds of over 75 cows). Dairy farming is thus one of the few remaining stable family business enterprises; indeed, it is a way of living as well as a way of making a living, with corresponding far-reaching implications for national stability (Chs. 10, 16, 25). It is generally agreed that national welfare (health, soil fertility, population stability) demands that everything should be done to maintain a prosperous dairy industry.

While the production of pork, beef, egg, requires less human labor in proportion to food yield than the production of milk[2] the dairy cow is far more efficient in converting cattle feed into human food than are other farm animals in converting feed into meat or egg. The energetic efficiency of milk production in superior dairy cattle is 33 per cent, contrasted to about half this level, 17 per cent, for egg production in comparable superior fowls, and 5 to 15 per cent for meat production (Chs. 1, 3, 22, 23). The energetic efficiency of milk production is so much greater that in spite of the greater labor cost of milk production the current price of egg and meat is about $1.10 per pound of dry matter, whereas the price or whole fluid milk comes to about 50 cents per lb of dry matter and of non-fat dry milk (dry skim milk), only 14 cents per lb. Moreover, methods are being developed to reduce the human labor involved for milk production by greater use of better machines and by the use of larger animals of higher dairy merit (Ch. 22).

Furthermore, cattle consume roughage which swine and poultry cannot consume and, unlike non-ruminants, synthesize by way of rumen micro-organisms complete nutrient proteins from incomplete feed protein and virtually all the B vitamins (Ch. 20). The milk nutrients are thus, in part, obtained in the nature of a windfall, from material which is otherwise nutritionally useless.

Dairy cattle now consume[3] 91 per cent of all the silage consumed by farm animals, 53 per cent of the hay, 38 per cent of the other dry roughages, and 38 per cent of the pasture. These are feeds which cannot be used by man or even by swine or poultry. Dairy cattle consume only 19 per cent of the grain and other concentrate feeds. Swine, however, consume 48 per cent of all the corn or 35 per cent of all the concentrate feeds and except for about 2 per cent pasture, no roughage. Poultry consume 21 per cent of all concentrate feeds and for about 1 per cent pasture, no roughage. Speaking very generally—the feed units are not really equivalent for different farm animals—dairy cattle consume 34 per cent of all the feed consumed by farm livestock, beef cattle 20 per cent, sheep and goats 7 per cent, horses and mules 14 per cent, swine 15 per cent, poultry 9 per cent. These figures give a rough idea of the relative magnitude of the dairy industry from the viewpoint of use of raw material.

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[1] U. S. consumers spend over 3½ billion dollars a year for milk and dairy products, and the dairy industry employs (1938) "four times as many people as the railroad industry, fifteen times as many as the telephone industry, nineteen times as many as the automobile industry, and one out of every 15 U. S. families is dependent on milk for a living." See Table 21.7.

[2] The annual labor of milking and caring for a cow producing 5000 lbs milk, and growing her feed, is estimated to be 160 hours; for producing a 400-lb beef steer, 32 hours; for raising a 5-pig litter to 125 lbs per pig, 75 hours. On this basis, the food-*energy* return index *per man-hour* is 100 for the milk, 219 for the hog, and 305 for the steer; the food-*protein* return *per man-hour* is 100 for milk, 98 for hogs, and 112 for beef.—O. H. Brownlee, "Putting Dairying on a War Footing," Iowa State College, 1943.

[3] Jennings, R. D., U. S. D. Agr. Circular 670, 1943.

21.2: Nutritional importance of milk. Unlike other foods which he had to learn to consume, man, in common with other mammals, is a born milk consumer. Milk was evolved through the ages specifically for the nutrition of infant mammals, for bridging the gap between the dependent intrauterine and the independent adult life (Sect. 7.2). Milk from all species contains the same nutrients, although in different proportions. Finding milk good, man domesticated convenient mammals for furnishing him with milk throughout his life.

Having been developed for nourishing rapidly growing yet delicate and toothless infants, milk has unique physical and nutritional properties. Milk is bland, soothing, fluid, yet highly nourishing; hence its use as food during "melancholy"[4] and other disturbances, especially digestive, such as ulcer, for which milk is often used as a virtually exclusive diet[5].

Milk is commonly thought of as a "drink," but this must not lead one to the mistaken idea that fluid milk has less solids than some "solid" foods. Indeed, the opposite is frequently true. Thus, whereas the solid content in fluid milk is about 13 per cent, that in turnips is only 9 per cent, in tomatoes 6 per cent, in lettuce 5 per cent. Milk is, of course, easily made "solid" by treating it with rennet or by simple souring, both of which may be followed by "baking." The writer recalls the pleasant flavors and tastes of many sour-milk dishes partaken while visiting in the Balkans, especially in Belgrade, where "Bulgaricus Milk," made famous by Metchnikoff as a life prolonger, is so widely used by all classes of society. It is, of course, the nutrients in milk rather than the bacteria that prolong life (see, however, Rettger[37] below). Bulgaricus and other types of milk-souring destroy dangerous bacteria, thus making the milk safe as food. This is the major (even if unconscious) reason for the use of soured (or boiled) milk in much of Europe where hygienic conditions are not satisfactory and bovine tuberculosis is very common.

The nutritional importance of milk is indicated by the fact that a quart of cow's milk a day furnishes (Table 21.1) an average man (of 70 kg or 154 lbs) approximately all the needed fat, calcium, phosphorus, riboflavin, one-half of the needed protein, one-fourth of the needed energy, over one-third of the vitamin A, one-fifth of the thiamine and ascorbic acid, considerable amounts of nicotinic acid and choline, and other factors, and, with the exception of iron, copper, manganese and magnesium, which are low in milk, all the needed minerals. (The protein in a quart of milk is roughly equivalent to that in 5 ounces of meat or fish, or 5 large eggs, or 4 ounces of American cheese, or 16 slices of bread. The energy of a quart of milk is roughly equivalent to that in $\frac{3}{4}$ lb of meat, or 8 eggs, or 2 lbs of potatoes.)

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[4] "Milk is especially good for them which be oppressed with melancholy, a common calamity of students."—Thomas Cogan, 1584.

[5] Shay, H., *Jour. Am. Med. Assoc.*, **120**, 740 (1942).

These estimates do not fully indicate the contribution of milk to the average diet because of the unique *supplementary* value of milk to other foods (Sect. 20.4). For example, when growing pigs are fed only cereal, about 30 per cent of the cereal protein is utilized for growth; but if milk is added to the diet (liquid milk equal in weight to the cereal weight) 60 per cent of the protein is utilized for growth[6] because of the supplementary effect of the protein and other constituents of milk.

Dramatic results of broad social significance were reported on the supplementary value of milk on growth of children, especially those by Dr. Corry Mann[7]. His boys were receiving a diet rated as adequate, but Dr. Mann wanted to see what an extra glass of milk at meals (a pint per day) would do. Records were kept of half of the group on their usual diet, and of an equal number who received the milk supplement. The result was that while the "control" boys gained 4 lbs in weight and 1.8 inches in height, the milk-supplemented group gained 7 lbs and 2.6 inches. "The casual visitor would never fail to recognize the boys receiving the extra milk," said Dr. Mann; "they were obviously more fit."

The spectacular growth-accelerating effect of milk on weight and especially on height (skeleton growth, see Fig. 21.1b) is perhaps due largely to the richness and availability of calcium in milk. In Mann's experiments the addition of casein equivalent to that given in milk and margarine equivalent to the butterfat in the milk did not increase the height as did whole milk. Leighton and Clark[7] found that *skim milk increased growth in height as much as whole milk.* These observations lead to the conclusion that the calcium in milk is a major factor in increased growth of the skeleton. Ordinary diets are more often deficient in calcium than in any other nutrient, and are thus made good by milk.

These observations on the remarkable influence of *skim milk* supplement on growth suggest the need of elucidating a current problem in the dairy industry.

As previously noted, there is enough milk produced in the United States to furnish a quart per capita per day, the optimal level of milk intake. Half of this milk, however, is used for manufacturing butter (about 18 lbs per capita per year) and cheese (about 6 lbs per capita per year). The popularity

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[6] Steenbock, H., and Hart, E. B., *J. Biol. Chem.*, **38**, 267 (1919); **42**, 67 (1920); Wis. Agr. Exp. Sta. Bull. 342, 1922.

[7] See, *inter alia*, Mann, H. C. Corry, "Diet for boys during the school age." Special Report Series 105, Medical Research Council, London, 1926; also, Mann, *J. Roy. Inst. Public Health and Hyg.*, **2**, 486 (1939), and *Nutr. Abst. & Rev.*, **9**, 686 (1939). See also Palmer, G. T., *Am. J. Pub. Health*, **12**, 134 (1922); Sherman, H. C., and Campbell, H. L., *J. Am. Chem.*, **60**, 5 (1924). Rose, M. S., and MacLeod, G., *J. Biol. Chem.*, **66**, 847 (1925). Orr, J. B., *Lancet*, **1**, 202 (1928). Leighton, G., and Clark, M. L., *Id.*, **1**, 40 (1929). Morgan, A. F., *et al.*, *Am. J. Dis. Child.*, **32**, 655 (1926); **33**, 404 (1927); **36**, 972 (1928).

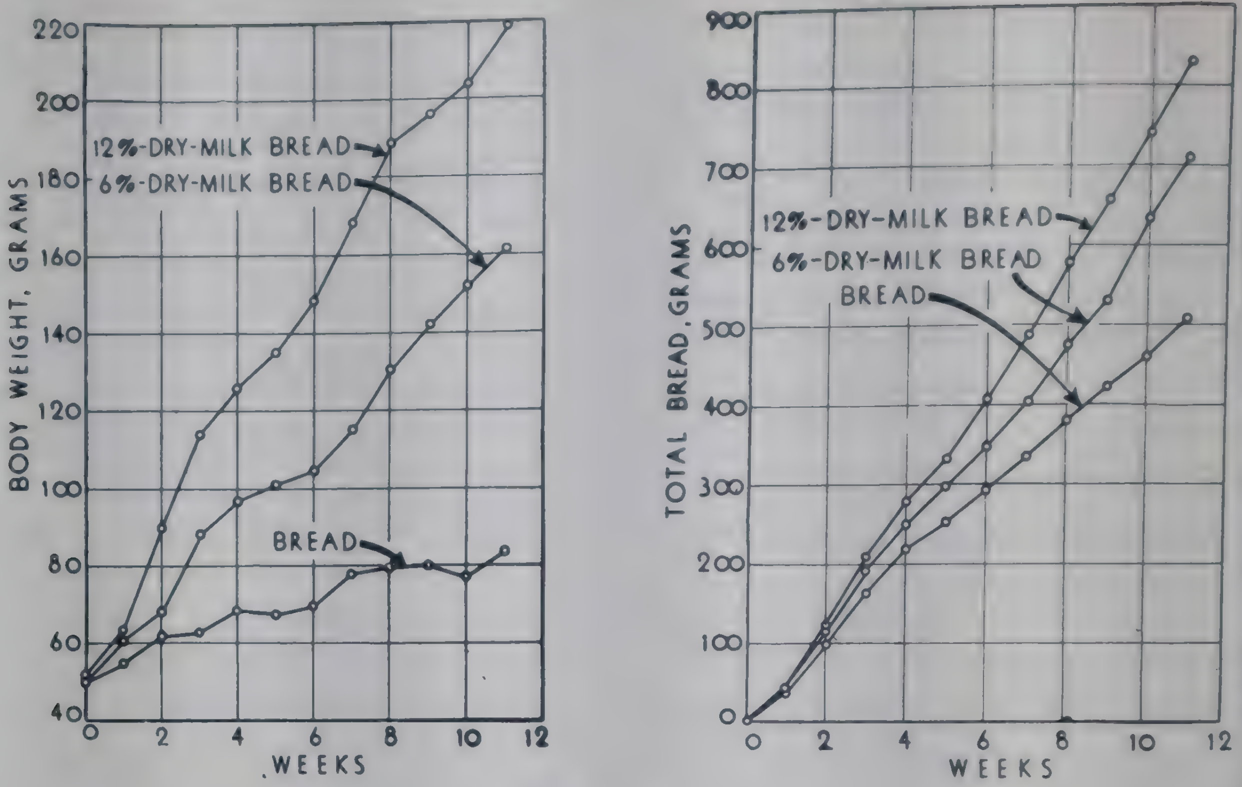

Fig. 21.1a

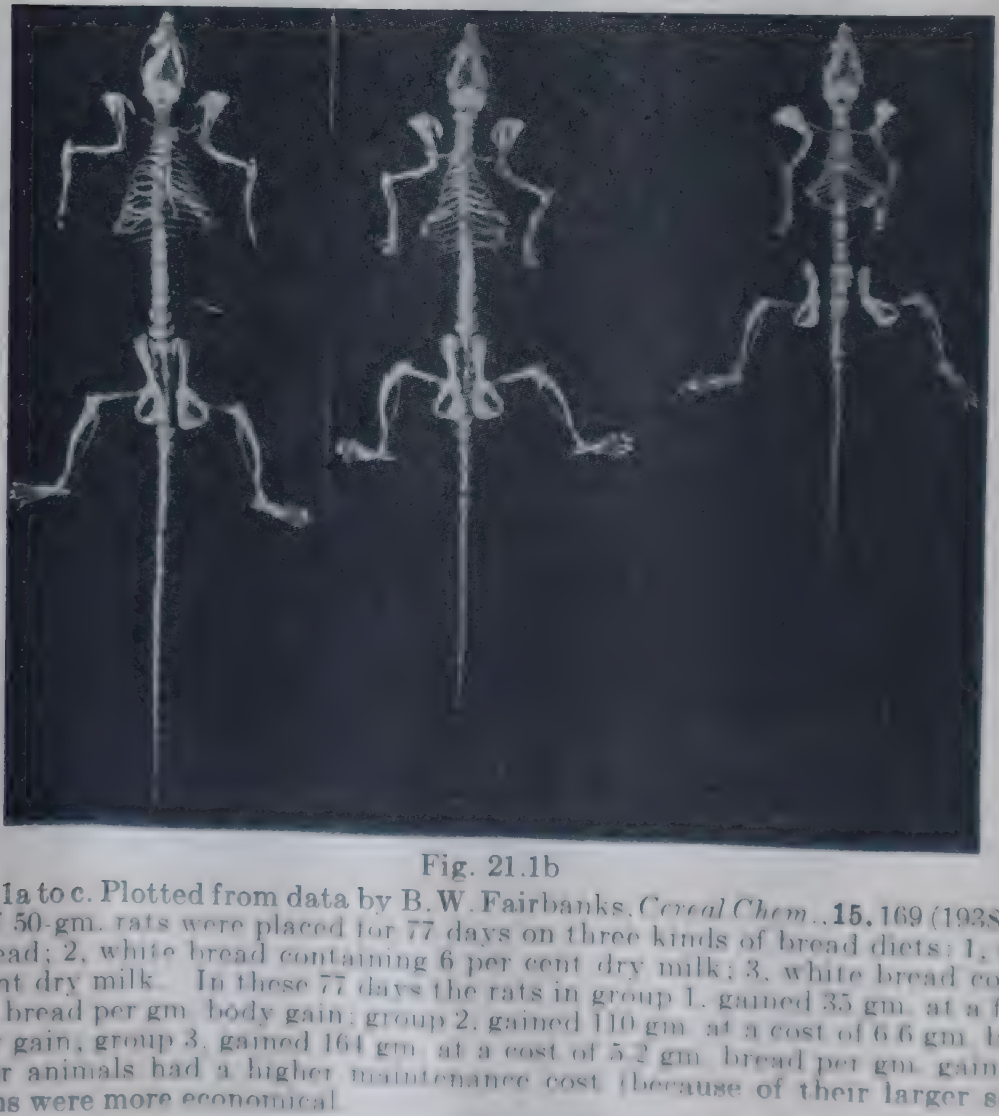

Fig. 21.1b

Fig. 21.1a to c. Plotted from data by B. W. Fairbanks, *Cereal Chem.*, **15**, 169 (1938). Three groups of 50-gm. rats were placed for 77 days on three kinds of bread diets: 1, ordinary white bread; 2, white bread containing 6 per cent dry milk; 3, white bread containing 12 per cent dry milk. In these 77 days the rats in group 1. gained 35 gm. at a food cost of 25 gm. bread per gm. body gain; group 2. gained 110 gm. at a cost of 6.6 gm. bread per gm. body gain, group 3. gained 164 gm. at a cost of 5.2 gm. bread per gm. gain. While the larger animals had a higher maintenance cost (because of their larger size), yet their gains were more economical.

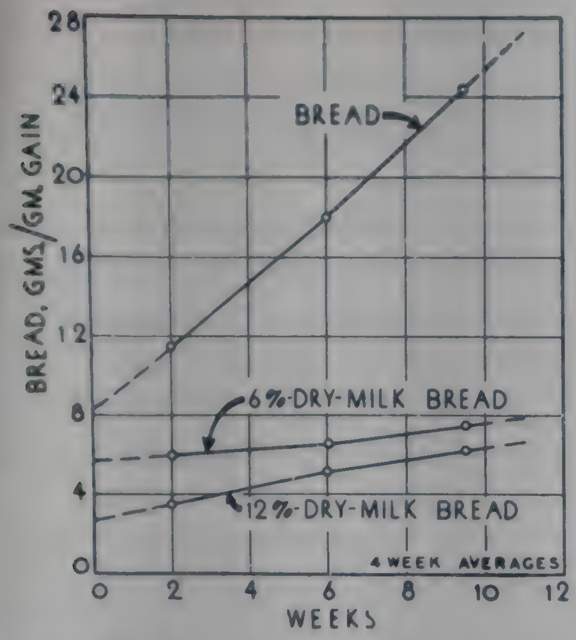

Fig. 21.1c.
See legend on page 796.

of butter is, of course, due to its high nutritive value, its very tasty flavor, ease of its manufacture from cream and ease of preservation. The advent of the mechanical cream separator and the Babcock tester made it easy for the farmer to separate cream from milk to any fat percentage, and for the buttermaker to pick up the cream for butter manufacture. The skim milk was fed to the swine and poultry, for, as previously noted, milk, even skim milk, is an excellent supplement to cereals normally fed to these animals.

But it is also good for man to supplement his cereal with milk, even skim milk; and as long as there is not enough of a given food for man, it is, usually, wasteful to feed this food to livestock. For example, per unit dry matter, milk is nutritionally equivalent to meat; yet when fed to animals only about ten per cent of the milk solids is recovered in the form of meat solids[8] (Ch.3). Thus it is estimated that about 50 billion pounds of skim milk[9] (about 4 billion pounds non-fat dry-milk solids) perhaps 40 per cent of the total milk solids produced in the United States, said to be equivalent to the protein in 200 million beef steers[10], is diverted from human use, and 90 per cent of it is wasted as far as human nutrition is concerned. (There are, of course, exceptions, as when a little skim milk may be the limiting factor in a ration for chickens in egg production.)

More specifically, Krauss[11] reported that if United States milk production were completely utilized as human food, the non-fat part of the milk would satisfy the protein needs of 67 million persons, the riboflavin needs of 130 million persons, the calcium needs of 165 million persons; but that according to the present practice of feeding the skim milk and whey to livestock, etc., only half of these nutrients are utilized for human consumption. This huge waste of food is due to a serious misunderstanding about the nutritive value of defatted or skim milk. Let us, therefore, discuss this problem briefly.

[8] Abbott, J. S., *Am. J. Public Health*, **30**, 237 (1940).

[9] "Consumers' Guide," U. S. D. Agr., July, 1939.

[10] Rose, W. C., Jones, D. B., Morse, W. J., and Pollock, R. C., "The Nation's Protein Supply." Nat. Research Council Reprint and Circular Series, No. 114, Aug. 1942.

[11] This discussion is based mostly on Krauss, W. E., Address American Dry Milk Institute, April 14, 1943; Reed, O. E., Address National Dairy Council, June 28, 1943.

The composition of whole milk is given in Table 21.1 in the form of a comparison between the nutritional needs of an average adult person and the nutrients furnished in a quart of average market milk (slightly modified from Krauss[11]).

Table 21.1 shows that a quart of average milk (2.15 lbs or 4 glasses of 8 fluid ounces each) supplies to an average moderately active man approximately the following percentages of the nutrient standard: 150 per cent of the calcium, 70 per cent of the riboflavin and phosphorus, 50 per cent of the protein, 40 per cent of the vitamin A[12], 25 per cent of the ascorbic acid[13], 20 per cent of the calories and thiamine, 5 to 10 per cent of the iron, nicotinic acid, and vitamin D[12].

The milk energy is seen (Table 21.1) to be equally divided between fat, 330 Calories (37 gm fat per quart) and non-fat, 330 Calories (49 gm lactose and 34 gm protein per quart). (The energy value of whey is about 270 Cal per quart or per kg.) The milk *fat* thus supplies half the milk energy, the vitamins A and D, and much of the flavor; the *non-fat* part of the milk, the *skim milk*, supplies the other half of the energy, the proteins of high biological value, calcium, riboflavin, phosphorus, iron, ascorbic acid, thiamine, nicotinic acid, and apparently some unknown growth factors (Reed). It is thus clear that in evaluating milk as a food, at least as much value should be placed on the non-fat as on the fat portion.

A slow transition may be taking place in the dairy industry as a result of the war and its associated world-wide food shortage[14]. Ways will, no doubt, be found to save the skim milk, buttermilk, and whey for the human dietary.

[12] The vitamin-A value of milk varies with the carotene content of the feed. Fresh pasture yields milk highest in vitamin A content, followed by well preserved silage, then by hay, especially if dried by rapid-drying methods.—Hilton, J. H., *et al.*, *J. Dairy Sci*, **16**, 355 (1935). For the influence of feeding high vitamin A shark-liver oil on the vitamin A in milk, see Jensen, C., *et al.*, *J. Dairy Sci*, **25**, 1931 (1943). Likewise, the vitamin D of milk varies with the vitamin D content in the feed as well as with *sunshine*.

[13] There is a large literature on the ascorbic acid content of milk. The ascorbic content in cow's milk is about one-sixth and the iron content about one-third of that in woman's milk but the riboflavin content of cow's milk is about five-fold that of woman's milk. Heating in copper dishes destroys ascorbic acid. To save ascorbic acid in sterilization, heat the milk to the boiling point *very* quickly (to destroy ascorbic acid oxidase) then boil for three minutes. The ascorbic acid content of unpasteurized milk ranged from 17 to 37 mg, average 26 mg liter, for individual cows and 13 to 19 mg liter in plant composites before pasteurization and 16 to 17 mg liter after pasteurization. [C. H. Whitnah, *et al.*, *J. Dairy Sci.*, **19**, 373 (1936); **20**, 9 (1937)]. Other reports: 20 mg ascorbic acid liter [P. F. Sharp, *Science*, **84**, 461 (1936)]; mixed milk before pasteurization ranged month to month from 14-22 (average 17.3 mg liter) and after pasteurization 7.8–19.0 mg liter [A. H. Holmes, *J. Am. Diet. Assn.*, **15**, 363 (1939)]. Some authors claim an ascorbic acid peak for summer milk, others for winter milk, yet the character of the cow's feed does not influence the ascorbic acid content in milk [Holmes, *J. Nut.*, **17**, 187 (1939); **26**, 337 (1943)]. The ascorbic content of human milk varies with the diet, but it is about 60 mg qt. [King, C. G., *et al.*, *J. Nut.*, **11**, 599 (1936)]. The reports vary similarly for the other vitamins. Borsook suggested that milk should be enriched with crystalline thiamine as it is now frequently enriched with vitamin D.

[14] The food shortage referred to applies to most of Asia and Europe but not to the United States, where malnutrition is due to ignorance and economic factors rather than to national lack of food as such. Indeed, the 1942 agricultural production schedule supplies protein adequate to feed 183 million persons (furnishing 81 lbs protein per capita per year or 73 gm per capita per day), whereas there are only 134 million persons in the United States. Rose, W. C., *et al.*[16]

Instead of separating the milk on the farm and feeding the skim milk to livestock, the creameries and cheese factories may take the whole milk and develop facilities for drying the skim milk, buttermilk, and whey[15]. The dry products may be sold in the form of capsules, wafers, or powder, perhaps variously flavored, on grocery shelves[16], in jars, cartons, and air-tight, moisture-proof envelopes. The packages could contain 4½ ounces (127 gm) solid whole milk, each equivalent to a quart of fluid whole milk, or the envelopes could contain a fourth of this, equivalent to a large glass of milk, or multiples of these amounts. When used for soups and baking, milk powder is said to yield products superior to fluid milk, since it is uncomplicated by the water in the milk. The recently developed food-compression machinery may be used for tableting milk solids, whole or defatted, to be consumed direct, as the very hard cheese in some parts of eastern Europe is consumed.

The organismic theory (Ch. 10) suggests that it would be better to consume whole milk than any of its parts, because it is probable that the various milk constituents supplement one another nutritionally. A given amount of whole milk has a higher physiologic energy value than the sum of its constituents taken separately at different times. The fat in the milk *supplements* the protein and the sugar in the milk. "It seems that nature has put lactose and milk fat together as an optimum combination for the young animal[17]." "Lactose has an as yet unknown effect on intestinal conditions which is counteracted by butterfat but not by corn oil." "Fortified oleomargarine did not give growth equal to butterfat when lactose was the sole carbohydrate in the diet. . . . Fortified oleomargarine gave growth equal to butterfat over a period of 6 weeks when . . . a mixture of carbohydrate (sucrose, starch, dextrine, lactose) was incorporated."

It would, then, seem best to consume the recommended or available quart of milk per capita per day in the form of whole milk, fluid or evaporated, as a bread "spread" made by evaporating milk to the consistency of butter, whole-milk cheese (including the whey solids[18]), or best used in bread making[19] as milk bread, and in soups[20], puddings, cakes, cookies, or in the form of a beverage, even as reconstituted milk[21].

[15] This is not a novel idea. See Eckles, C. H., *et al.*, "Milk and its products," p. 201.

[16] Since the above was written, Merrill O. Maughan (American Dry Milk Institute) kindly sent me an 8½-oz package of powdered whole milk, equivalent to the solids in 2 qts fresh milk, which is being marketed "experimentally" in some localities for about 26 cents a package (equivalent to 13 cents a quart fluid milk). It is apparently less expensive to dehydrate, package, and market dry milk from grocery shelves than to process and market fresh milk. Moreover, the powdered milk keeps for months. The package had the following inscriptions: "8½ ozs net wgt, just add water . . . makes 2 quarts of fine fluid milk. . . . For best results use within sixty days of purchase." The given analysis: 27% butterfat, 26.8% protein, 38.1% milk sugar, 5.88% ash, 2.25% moisture, 142 Cal per ounce (about 5 Cal/gm). The reconstituted milk has a slightly cooked taste somewhat similar to that of evaporated milk.

[17] Hart, E. B., Elvehjem, C. A., *et al.*, *J. Dairy Sci.*, **26**, 429 (1943); *Science*, **93**, 499 (1943); *J. Nut.*, **26**, 601 (1943).

[18] Velveeta cheese contains some of the whey solids. The composition of this cheese [as reported in the *Jour. Am. Med. Assn.*, **120**, 24 (1942)]: moisture, 43.1%; Calories per ounce, 90; fat, 23.4%; protein, 18.4%; carbohydrates, 10.1% (8.4% lactose); ash, 5.3%; calcium, 0.61%; phosphorus, 0.82%; salt, 1.8%; lactic acid, 1.2%.

[19] Cf. Mitchell, H. H., *et al.*, *Bakers' Weekly*, **114**, 27 (1942); *J. Nut.*, **25**, 585 (1943).

[20] The M.I.T. in cooperation with the Rockefeller Foundation and the Kellogg Foundation developed a dehydrated milk soup containing 10% milk solids. A cup of this soup supplies the daily needs of all the known vitamins and minerals.

[21] "Reconstituted milk," *Nut. Rev.*, **1**, 70 (1943).

While there can be no substitute for whole milk or for skim milk, claims are being advanced by the margarine industry that oleomargarine fortified with vitamins A and D to the butter level[22], flavored with diacetyl or related butter flavor, and colored to the butter level with carotene may be acceptable to *adult* consumers who cannot afford butter. The question of unsaturated fatty acids of the linoleic acid type does not, perhaps, enter the problem, since most vegetable fats are as rich in this type of fatty acid as butter; nor, perhaps, does the question of "digestibility" (in adults).[23] There are, however, short-chain fatty acids (Table 21.2) and other substances in butter not present in other fats, and butterfat stimulates growth in young rats[24, 25] and calves[26]. As previously noted, however, the superior growth on butterfat in milk over that on vegetable oil in skim milk may be due to the supplementary effect of milk sugar on butterfat[17]. Milk fat seems to go best with milk sugar and vegetable fat with vegetable sugar. If butterfat goes best with the other milk solids, it is safe to predict that a new butter "substitute" will be developed in due time by the enterprising American dairy manufacturers, namely, whole milk evaporated to the consistency of butter, properly flavored, and advertised for use as a "spread" in butter fashion.

The butter-margarine problem is now receiving much attention basically because of the growth of the vegetable-oil industry and technological advances in margarine and vitamin A production. No one argues against butter. The following statement is generally accepted. "Our nation has grown up with butter on its bread. Butter was eaten for its taste long before there was any knowledge of nutrition. We like it on our hot cakes and in countless other ways for its flavor alone. Butter will always be in demand because of its flavor and palatability. These characteristics are not duplicated by any other fat" (Reed). But the margarine industry is pushing its product; and the broader national problem is how to avoid wasting the precious nutrients in skim milk and buttermilk produced in buttermaking. (O. E. Reed, Chief of the Federal Bureau of Dairy Industry, phrased this problem, thus: "Our dairy industry is not operating on the most efficient basis for our national nutrition—we skim the cream from a lot of milk and we use only the cream or the fat.") The outcome of this controversy between two industries is uncertain, but it would seem wise for the dairy industry to develop profitable whole-milk "spreads"[27] (by the simple device of evaporating whole milk to the consistency of butter, perhaps adding "binder" and flavoring, and add further to tastefulness of the product by proper publicity) and whole-milk cheeses (including whey solids).

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[22] The vitamin A content of butter is between 5000 and 20000 I.U., average 15000 I.U. per pound [Dornbush, A. C., *et al.*, *Jour. Am. Med. Assn.*, **114,** 1748 (1940)]. The vitamin D content of butter is 50 to 500 I.U. per pound [Wilkinson, H., *Analyst*, **64,** 17 (1939)]. At the rate of 17 lbs butter consumption per year, the vitamin A furnished by butter is 600 to 700 I.U./day.

[23] For a review of the butter versus oleomargarine problem in 1942, see Council on Food and Nutrition, *Jour. Am. Med. Assn.*, **119,** 1425 (1942); **118,** 1469 (1942); **126,** 168 (1944).

[24] Hart, E. B., Elvehjem, C. A., *et al.*, *J. Biol. Chem.*, **122,** 381 (1938); *J. Dairy Sci.*, **23,** 181, 1201, 1205 (1940); **24,** 1027 (1941).

[25] Deuel, H. J., Jr., *Science*, **98,** 139 (1943), published evidence to the effect that the superior growth on milk fat is due to its superior flavor which caused the rats to consume more of the natural milk, and that flavoring the vegetable oil abolished the difference in growth rate. The problem is evidently still in the controversial stage. See also Deuel, *et al.*, *J. Nut.*, **27,** 107, 335, 339 (1944). The superior flavoring, diacetyl, referred to by Deuel is, however, not that of natural milk fat as consumed by infants (rats or other species), but is bacteriologically developed by buttermakers.

[26] Gullickson, T. W., *et al.*, *J. Dairy Sci.*, **22,** 471 (1939); **25,** 117 (1942).

[27] Grateful acknowledgments are made to all the author's (Dairy Department) colleagues for stimulating discussions and for especially valuable suggestions by E. R. Garrison and W. H. E. Reid. Since the above was written, K. G. Weckel, University of Wisconsin, assigned to the Wisconsin Alumni Foundation formula for a "dairy spread" containing 56% moisture, 26% butterfat, 16% non-fat milk solids, 1% salt,

The historical aspect of the nutritional importance of butterfat is generally known. Vitamin A was first discovered in milk fat[28], and the first severe cases of clinical xerophthalmia were described in children fed defatted milk[29]: "The eye-sight of the children was sold abroad with the butter[30]."

Milk fat is characterized[31] by a high content (7 per cent) of volatile fatty acids, mainly butyric and caproic, with small amounts of caprylic and capric, and related acids. This is indicated by Table 21.2[32, 33]. Vegetable fats and blood lipoids do not appear to contain fatty acids with less than 12 or 14 carbons. These short-chain fatty acids are apparently synthesized by the mammary gland, as there are none in blood.

The composition of milk fat varies with season, perhaps due to seasonal differences in the feed and also to temperature[34]. The summer (pasture) milk is richer in oleic acid, poorer in butyric and stearic, but the palmitic remains constant. This may, perhaps, contribute to the differences in nutritive value of summer and winter milks.

The phospholipids (about 0.05 per cent lecithin in average milk, 0.2 per cent in cream, 0.016 per cent in skim milk, 0.13 per cent in buttermilk, 0.07 per cent cephalin in milk) are not definitely related to the amount of fat. Cow's milk contains twice as much phospholipid and four times as much phosphorus as human milk. The cholesterol content of cow's milk is about 0.02 per cent and of butter oil 0.3 per cent; 18 per cent of the milk cholesterol is associated with the lactalbumin rather than with the fat.

The short fatty acid and other milk-fat peculiarities may or may not be of nutritional significance. There are no experimental data on this question. It seems unreasonable, however, to suppose that the mammary glands of all mammals would evolve mechanisms for the synthesis of these short-chain fatty acids (see table below) without serving some need.

As previously noted, fluid (market) milk contains about 13 per cent solids; hence milk at 13 cents a quart is equivalent to one cent per one per cent solids per quart. Assuming that a quart of milk contains 4.5 ounces (127 gm) of solids, then at 13 cents a quart, the milk solids come to 2.9 cents per ounce (28.3 gm) or 46 cents a pound (453.6 gm).

The market price of butterfat is about 50 cents a pound, and it has been suggested[35] that milk sugar (lactose) is worth no more than store sugar (sucrose), *i.e.*, 5 cents a pound. This gives the milk protein and minerals a monetary value of one dollar a pound. (*Note:* Meat protein is $1.00 a pound when meat is 20 cents a pound; cheese protein is 90 cents a pound when cheese is 30 cents a pound; egg protein is 75 cents a pound when egg is 30 cents a pound; bean protein is 13 cents a pound when beans are 10 cents a pound; white-flour protein is 10 cents a pound when white flour is 6 cents a pound[35].)

The above type of computation seems unfair because it omits the vitamins, trace elements, and unknown factors in milk, the optimal calcium-to-phos-

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9000 units per pound vitamin A from fish-liver oil, 3200 units per pound vitamin D from irradiated ergosterol, also cultured buttermilk flavor and lactic acid. The making of the spread involves the use of a vacuum pan, pasteurizer, and homogenizer.

[28] McCollum, E. V., and Davis, M., *J. Biol. Chem.*, **15**, 167 (1913). Osborne, T. B., and Mendel, L. B., *Id.*, p. 311.

[29] Bloch, C. E., *Am. J. Dis. Child.*, **27**, 139 (1924).

[30] Woods, Ruth, Borden's Review of Nutrition Research, Jan. 1943, p. 3.

[31] Bloor, W. R., "Biochemistry of Fatty Acids," Reinhold Pub. Corp., 1943.

[32] Hilditch, T. P., *Analyst*, **62**, 250 (1937).

[33] Hilditch and Longenecker, H. E., *J. Biol. Chem.*, **122**, 497 (1938); **139**, 727 (1941).

[34] Hilditch, T. P., *J. Soc. Chem. Ind.*, **60**, 305 (1941).

[35] Goodale, H. D., *Hoard's Dairyman*, **82**, 316 (1937). Prentice, E. Parmlee, letter.

phorus ratio[36], and the unique properties of milk sugar. Unlike sucrose, lactose passes the ileo-cecal valve and forms in the intestine an exceptionally favorable medium for the growth of *Bacillus acidophilus*[37] and related acid producers, thereby inhibiting protein putrefaction. By thus maintaining an acid reaction in the intestine, lactose, moreover, favors maximum calcium and phosphorus utilization (at least in the rat). It is known that (in the rat) the ricket-producing properties of some diets are repressed by supplementing with lactose[38]. The greater anti-rachitic value of woman's milk as compared to cow's milk is attributed to the higher lactose content of the former. Finally, lactose furnishes an important building stone, galactose (1 galactose + 1 glucose → 1 lactose), for the nervous system.

As previously noted, milk also contains phospholipids[39]—as lecithin, cephalin, sphingomyelin, cerebrosides—which undoubtedly have nutritional significance.

The unique value of milk in the national health program (Sect. 20.2) consists particularly in its *supplementary* value to the prevailing refined-cereal-potato-sweets diet, especially to those in the low-income group who cannot afford to buy meat, eggs, green vegetables, and fruit (Fig. 21.2). The daily consumption of a quart of milk may render almost adequate an otherwise inadequate diet.

A century ago, the per capita consumption of pure sugar was 8 pounds a year; now it is over 100 (112 in 1941)[40]. About 20 per cent of the total calories of the average consumer is furnished by sugar[41], and 30 per cent of the calories is furnished by white flour. The milling process has been so perfected that modern white flour is almost completely devoid of its mineral and vitamin "impurities." (The milling process removes $\frac{2}{3}$ of the iron, $\frac{1}{2}$ of the calcium, $\frac{3}{4}$ of the copper, $\frac{3}{4}$ of the thiamine, $\frac{3}{4}$ of the riboflavin, $\frac{3}{4}$ of the vitamin B complex and nearly all the manganese and magnesium.) The net result is a marginal diet in which 50 per cent of the Calories are derived from sugar and white flour, nearly devoid of minerals and vitamins, with corresponding marginal health[41]. Nervous manifestations associated with beri-beri and pellagra are said to be endemic in the United States[41], as are [42] ". . . among other signs and symptoms, moodiness, sluggishness, indifference, fear, and fatigue." The Stiebeling reports[43] ". . . reveal a large proportion of poor diets in peaceful America with its bursting granaries. . . . The diets were poor in vitamins A, D, and B_1 and in calcium. . . . When white flour and sugar provide 50 per cent of the calories . . . selection of a diet that can be called good . . . is almost impossible except for an expert."

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[36] McCollum, E. V., *et al.*, *J. Biol. Chem.*, **47**, 505 (1921). Sherman, H. C., and Hawley, E. E., *Id.*, **53**, 375 (1922). Sherman and Pappenheimer, A. M., *J. Exp. Med.*, **34**, 189 (1921).

[37] Rettger, L. F., *et al.*, "A treatise on the transformation of the intestinal flora with special reference to *Bacillus acidophilus*," Yale Press, 1921. "*Lactobacillus acidophilus* and its therapeutic applications," Yale Press, 1935.

[38] Bergeim, O., *J. Biol. Chem.*, **70**, 35 (1926). Kline, O. L., Keenan, J. A., Elvehjem, C. A., and Hart, E. B., *Id.*, **98**, 121 (1932). Outhouse, J., *et al.*, *J. Nut.*, **20**, 467 (1940).

[39] Kurtz, F. E., and Holm, G. E., "Lipids of milk." *J. Biol. Chem.*, **106, 717** (1934), and *J. Dairy Sci.*, **22,** 1011 (1939). Heinneman, B., "Relation of phospholipids to fat in dairy products," *J. Dairy Sci.*, **22, 707** (1939). Crane, J. C., and Horrall, B. E., "Phospholipids in dairy products," *Id.*, **25,** 651 (1942).

[40] Roberts, L. J., *Milbank Memorial Fund Quarterly*, **17,** 230 (1939).

[41] Lamborn & Co., sugar brokers, gave in their Oct. 22, 1943, publication ("Formula for sabotage of the sugar industry") an interesting example of "double talk" connecting (psychologically) the rise of Hitlerism, the decline of France, etc., with the opinion that Americans are consuming too much sugar. "The (nutritionists) weed is planted. It is of the spreading variety . . . Eventually there are literally millions saying parrot-like "they say that you don't need any sugar. . . ."

[42] "Vitamins and war," *Jour. Am. Med. Assn.*, **115,** 1198 (1940).

[43] Stiebeling, Hazel K., and Phipard, Esther F., "Diets of wage earners," U. S. Dept. Agr. Circ. 507, 1939, also *J. Nut.*, **19,** 21 (supplement) (1940). See also: Stiebeling and Ward, M. M., "Diets at four levels of nutrition," U. S. D. A. Circ. 296, 1933. Stiebeling, "Food budgets," U. S. D. A. Misc. Pub. 183, 1933; Carpenter, R. C., and Stiebeling, "Diet to fit income," U. S. D. A. Farmer's Bull. 1757, 1936. Orr, J. B., "Food, health, and income." Macmillan, 1936.

The dietary complications which worry physicians[42], food economists[43], and nutritionists[44] may be solved, as suggested by Sherman[45], McCollum[46], Rose[47], and others[48], by including in the diet a quart of whole milk a day. This milk corrects the faults of the "perversely" used impoverished foods. Moreover, milk can be made a carrier of the easily manufactured vitamins[49], as B_1, in the same manner as it is now often enriched with vitamin D.

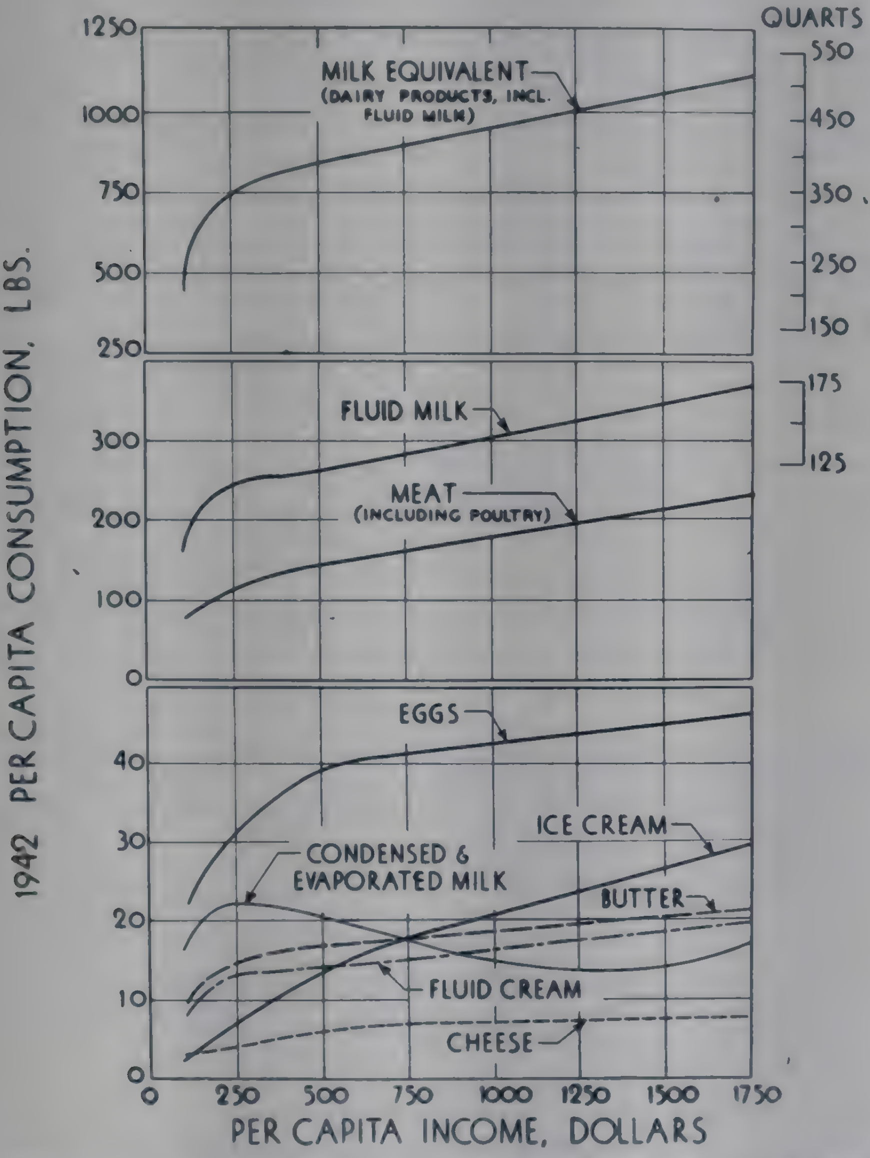

Fig. 21.2. Milk, meat, and egg consumption as related to income level. Modified from "The Dairy Situation", Bureau of Agricultural Economics, U. S. Dept. Agriculture, November, 1942.

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[44] "Symposium on the fortification of foods with vitamins and minerals," *Milbank Memorial Fund Quarterly*, **17,** #3, 1939. Contributors: Agnes Fay Morgan, Lydia J. Roberts, W. H. Sebrell, E. M. Nelson, Alonzo E. Taylor.

[45] Sherman, H. C., "Chemistry of food and nutrition," New York, 1938. Sherman, H. C., and Lanford, Caroline Sherman, "Essentials of nutrition," Macmillan, 1940.

[46] McCollum, E. V., Orent-Keiles, E., and Day, H. G., "The newer knowledge of nutrition," New York, 1939.

[47] Rose, Mary S., "The foundation of nutrition," New York, 1938.

[48] Brody, S., "Nutrition," *Ann. Rev. Bioc.*, **4,** 392 (1935).

[49] Borsook, H., "Vitamins," Viking Press, 1940.

To be sure, milk is not suitable as an *exclusive* diet after the normal weaning age. The amounts of iron, copper, and manganese salts are inadequate in milk when fed to adult rats as an exclusive diet. (The young are born with iron and copper reserves in the liver to meet their needs during the suckling period.) But when the milk is supplemented by these salts, rats[50] and dogs[51, 51] may be maintained almost indefinitely (for four generations at least) on the exclusive (mineralized) milk diet. They also reproduced, although at a lower rate[50, 51], on this diet. Calves[52] were also grown on this mineralized milk diet for at least two years, but in addition to iron, copper, and manganese, magnesium had to be added to the milk[53]. Milk is also inadequate in vitamin C when fed to species dependent on dietary ascorbic acid.

Fortunately, whole cereal (such as whole-wheat bread) supplements the milk deficiencies in a practically perfect manner (except for ascorbic acid). This was demonstrated by Sherman (Sect. 18.2.4), who maintained many generations of rats on an exclusive whole milk-whole wheat (and salt) diet. Sherman had two diets differing in the milk-to-wheat ratios: (1) $\frac{1}{6}$ dry whole milk and $\frac{5}{6}$ whole wheat; (2) $\frac{1}{3}$ dry milk and $\frac{2}{3}$ wheat. In comparison to a good stock diet, the rats on diet (1) performed *satisfactorily* in growth, health, reproduction, and longevity; on diets (2) they performed *excellently* in growth, health, and longevity. The most striking observation is that the rats on diet (2) matured earlier, lived longer and retained their vigor to a more advanced age. This result leads to the tentative conclusion that a whole milk-whole cereal diet (supplemented in the case of man with raw cabbage or raw or canned tomato or citrus for vitamin C) in which milk furnishes about $\frac{1}{3}$ to $\frac{1}{6}$ of the Calories (as when a daily quart of milk is consumed) is nutritionally complete. Taylor[54] suggested the combination of milk and bread into a milk-bread, which is less expensive than milk *and* bread. It seems agreed that most people are alike in needing milk; unfortunately, they are not alike in their ability to get it, and the basic problem is how to bring it within their means (Fig. 21.2).

21.3: Composition of milk. This section is not concerned with the details of the chemical composition of milk on which there are extensive reviews[55], but with some of its general features.

Bunge[56] suggested that the chemical composition of milk in different species is correlated with the chemical composition of the new-born animal. This correlation, if any, does not appear to be striking. More striking is the parallelism between milk composition and maturing speed of the new-born mammal, as exemplified by Table 21.3 mostly from Abderhalden[57], who called attention to this relation. (This table is modified and extended on the basis of the newer literature[55].)

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[50] Richardson, L. R., and Hogan, A. G., *J. Nut.*, **19**, 13 (1940).

[51] Elvehjem, C. A., *et al.*, *J. Nut.*, **20**, 433 (1940).

[52] For extensive reviews see Herman, H. A., Univ. Mo. Agr. Exp. Sta., Res. Bull. 245, 1936. Savage, E. S., and McCay, C. M., *J. Dairy Sci.*, **25**, 595 (1942). Krauss, W. E., Ohio Agr. Exp. Sta. Bull. 477, 1931.

[53] Duncan, C. W., Huffman, C. F., and Robinson, C. S., *J. Biol. Chem.*, **108**, 35 (1935). Wise, G. H., Gullickson, T. W., and Petersen, W. E., *J. Dairy Sci.*, **22**, 573 (1939), and **23**, 997 (1940).

[54] Taylor, Alonzo, *Jour. Am. Med. Assn.*, **81**, 892 (1923).

[55] Rogers, L. A., Associates of, "Fundamentals of dairy science," Reinhold, 1935. Davies, W. L., "The chemistry of milk," New York, 1939. Shohl, A. T., "Mineral metabolism," New York, Reinhold, 1939. "Food and Life," the 1939 Yearbook of Agriculture, U. S. D. A., Washington, 1939. Reviews by C. A. Cary, *et al.*, p. 649, and L. P. Earle, p. 501. Biennial Reviews of the Progress of Dairy Science in the *J. Dairy Reserach*, U. S. D. A.: Farmers Bull. 1359, 1923. Geiling, E. M. K., *et al.*, *J. Biol. Chem.*, **134**, 71 (1940) (dolphin). Himwich, H. E., *et al.*, *Proc. Soc. Exp. Biol. and Med.*, **48**, 133 (1941) (monkey). See also dairy textbooks, particularly Petersen, W. E., "Dairy science," Lippincott, 1939, and Eckles, C. H., "Milk and its products," McGraw-Hill, 1929. Other references are cited in the text.

[56] Bunge, G., *Z. Biol.*, **10**, 326 (1874). Bunge, G., "Physiological and pathological chemistry," Philadelphia, 1902.

The relation between milk composition and maturing rate is complicated by many factors, evolutionary and physiologic. The milk of the ass, horse, and man is abundant in water (90 per cent) and sugar, but poor in protein and fat. The milk of the reindeer and marine mammals is very concentrated. The situation is too complex for a simple generalization, although, no doubt, speed of growth, composition and physiologic age (Ch. 19) of the young at birth are important factors in determining the evolutionary trend of milk composition. The method of obtaining the milk influences the *apparent* composition.

It is remarkable that the composition differences are no greater than they are. All milks contain the same constituents, although the proteins differ immunologically[58]. Thus persons allergic to cow's milk can take goat's milk without any ill effects.

In spite of the quantitative differences in composition of the milk of different species, man and most farm and laboratory animals thrive on cow's milk. While goats (kids) make exactly the same growth per Calorie on cow's as on goat's milk[59], calves are said[60] to react unfavorably to goat's milk; and while horses (foals) are said to react unfavorably to undiluted cow's milk, they thrive on undiluted goat's milk, although goat's and cow's milk have the same quantitative composition. The differences may be associated with differences in permeability of the digestive tract lining to some of the proteins of goat's and cow's milk, with consequent allergic reactions[61].

But even in the same species there is considerable difference in the quantitative composition of milk, indicated by the following cattle-breed-difference data, on small groups of animals, from Overman *et al.*[62]

Breed Differences in Composition of Milk (small groups of animals).

Cattle, breed	Means of percentages of components							
	Fat	Protein	Lactose	Ash	Solids	Water	Solids-not-fat	Specific Gravity
Ayrshire	4.1	3.6	4.7	0.68	13.1	86.9	9.0	1.0317
Brown Swiss	4.0	3.6	5.0	0.73	13.4	86.6	9.4	1.0318
Guernsey	5.2	4.0	4.9	0.74	14.9	85.1	9.7	1.0336
Holstein	3.5	3.4	4.8	0.68	12.5	87.5	9.0	1.0324
Jersey	5.2	3.9	4.9	0.70	14.7	85.3	9.5	1.0332
Guernsey-Holstein	4.4	3.8	4.9	0.72	13.8	86.2	9.4	1.0330
Average	4.4	3.7	4.9	0.71	13.7	86.3	9.3	1.0326

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[57] Abderhalden, E., *Hoppe-Seylers Z. Physiol. Chem.*, **26,** 489 (1898); **27,** 356 and 408 (1899).

[58] Wells, H. Gideon and Osborne, T. B., *J. Inf. Dis.*, **29,** 200 (1921). Nelson, J. B., Univ. Mo. Agr. Exp. Sta. Res. Bull. 68, 1924.

[59] Gamble, J. A., Ellis, N. R., and Besley, A. K., U. S. D. A. Tech. Bull. 671, 1939.

[60] Earle, I. P., "Food and life."[55]

[61] Ratner, B., *Am. J. Dig. Dis. and Nut.*, **2,** 324 (1935).

[62] Overman, O. R., Garrett, O. F., Wright, K. E., and Sanmann, F. P., Univ. Ill. Agr. Exp. Sta. Bull. 457, 1939.

There are, moreover, differences in composition within the breed as indicated by the following table (Overman, *et al.*).

Breed	Maximum and minimum percentages of milk constituents						
	Fat	Protein	Lactose	Ash	Solids	Water	Solids-not-fat
Ayrshire	2.9–5.7	2.9–4.6	2.4–6.1	.58–.85	10.6–15.8	89.4–84.2	7.2–10.4
Brown Swiss	2.9–6.5	2.6–5.7	3.7–6.7	.64–.99	11.4–17.3	88.6–82.7	8.0–11.4
Guernsey	3.7–7.7	2.7–5.5	3.6–5.8	.60–.85	12.1–17.9	87.9–82.1	8.2–11.1
Holstein	2.6–6.0	2.4–6.5	4.0–5.7	.56–.86	10.7–17.6	89.3–82.4	7.8–11.9
Jersey	3.3–8.4	2.9–5.8	2.7–5.7	.57–.82	11.0–11.7	89.0–88.3	7.7–11.1
Crosses	2.7–7.5	2.7–6.3	3.0–6.0	.58–.94	10.6–17.9	89.4–82.1	7.9–11.7
All samples	2.6–8.4	2.4–6.5	2.4–6.7	.56–.99	10.6–17.9	89.4–82.1	7.2–11.9

The caloric value of milk, of course, varies with its composition, especially with its fat percentage. Gaines suggested that milks of different fat percentage be converted into milk containing 4 per cent fat, designated FCM, which has a heat value of 750 Cal per kg, or 340 Cal per lb. According to Gaines[63],

$$FCM = 0.4M + 15F$$

M is weight of milk and F is weight of fat, all in the same units, and FCM is milk corrected to 4 per cent fat (see Table 22.3 for details).

The Gaines formula is based on the following combustion values per gram of milk constituent: 9.253 Cal for fat, 5.853 for protein, 3.693 for lactose; one kilogram of 4 per cent milk contains 750 Cal and 37 gm protein on the basis of 50 mg protein per Cal. The ratio of protein to energy is nearly constant, 43 to 49 mg protein per Cal, regardless of the fat percentage in milk.

The combustion energy of 4 per cent goat's milk[64] is virtually the same as of 4 per cent cow's milk: 342 Cal per lb for goat's milk, and 343 Cal for cow's milk. The combustion value of 3 samples of woman's milk was reported to be[65] 660, 680, and 770 Cal per liter.

It is often convenient to represent milk composition in terms of percentages of the total solids, or the nitrogen in terms of total nitrogen, as follows[66].

	Percentages in terms of the milk solids				Percentages in terms of total N		
	Fat	Protein	Lactose	Ash	Casein N	Albumin N	Non-protein N
Low-protein ration (N.R.1:13)	28.6	24.8	40.5	5.5	77.5	18.2	4.2
High-protein ration (N.R.1:2)	28.2	26.1	41.2	5.8	71.1	20.5	8.4

Species Differences in the Distribution of Nitrogen in Milk[58]

Species	Nitrogen in milk as percentage of total N					Ratio of Albumin + Globulin N to Casein N	Gms. N in 100 cc Skim Milk
	Casein N	Globulin N	Albumin N	Total Protein N	Non-protein N		
Saanen & Toggenburg goats	71	8.2	13.2	92	8.1	0.30	0.52
Holstein cows	76	8.5	9.6	94	6.2	0.24	0.50
Jersey cows	81	5.5	9.3	96	4.5	0.19	0.64
Human (one sample)	41	15.0	27	84	16	1.0	0.18

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[63] Gaines, W. L., Ill. Agr. Exp. Sta. Bull. 308, 1928. Overman, O. R., and Gaines, W. L., *J. Agr. Res.*, **46**, 1109 (1933).

[64] Peterson, V. E., and Turner, C. W., *J. Nut.*, **17**, 293 (1939).

[65] Shukers, C. F., *et al.*, *J. Nut.*, **5**, 127 (1932).

[66] Perkins, A. E., Ohio Agr. Exp. Sta. Bull. 515, 1932.

Incidentally, Perkins' table[66] shows that the dietary protein level may influence the percentage distribution of protein and especially non-protein nitrogen in the milk.

The table of Gamble, Ellis, and Gross[59] shows that in terms of percentage of total nitrogen, goats and cows have nearly the same composition, but human milk contains about half the casein, and double the albumin, globulin, and non-protein nitrogen as cow's or goat's milk. This may be associated with the younger physiologic age of human infants than those of cows or goats, since the non-casein nitrogen of milk is more closely related to blood nitrogen than is the casein nitrogen; and judging by the composition of colostrum, the younger the physiologic age of the newborn, the richer the milk in noncasein nitrogen.

The data of Gamble, Ellis, and Besley apparently show closer agreement in quantitative composition between goat's and Holstein-cow's milk than between Holstein and Jersey cow's milk, in spite of differences in mature weight, rate of physiologic maturation and growth, and different evolutionary history. This is also shown in the following summary of the species differences in the composition of milk.

	Fat (%)	Protein (%)	Lactose (%)	Ash (%)	Water (%)	Ca (mg %)	P (mg %)	Fe (mg %)	Cu (mg %)
Goat	3.5	3.1	4.6	0.79	88.3	114	98	0.072	0.053
Holstein cow	3.4	3.2	4.6	0.70	88.2	106	88	0.072	0.057
Jersey cow	5.3	3.8	4.7	0.73	85.7	117	101	0.088	0.058
Human[67]	3.5	1.3	7.5	0.2	88	34	15	0.2	0.05
Rat[68]	15	12	2.8	1.5	69	349	270	0.7	0.7
Dog[69]	8.3	7.5	3.7	1.2	77	289	240		

The rate of growth of suckling rats and human infants was almost identical per Calorie intake of goat's and Holstein's milk.

It is interesting to note that in spite of the enormous differences in the percentages of calcium and phosphorus in the milk of cow, rat, and dog, the Ca:P ratio is 1.2, the same in all. In human milk, the ratio is 2.3. These unusually high Ca:P ratios, rarely found in other foods, are very favorable for calcium assimilation. Milk is thus the best nutritional source of calcium, not only because of its richness in calcium, but also because of the favorable Ca:P ratio.

Summarizing, the qualitative composition of different milks is chemically (not always immunologically) the same, but different in the proportions between the constituents. While the composition tends to vary with the rate of maturing of the newborn animal, other factors confuse this relation.

21.4: Physico-chemical aspects of lactation. (See Sect. 7.2 for hormonal aspects.) The concentration of some substances, such as urea[70], is the same in milk and blood; the concentration of most constituents in milk differs from that in blood. Thus[71], in comparison to blood, cow's milk contains 40 times as much sugar[72] on a molar basis, and 80 to 90 times on a gravimetric basis[73]; 20 times as much fat, 14 times as much calcium, 7 times as much

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[67] Macy, I. G., *et al.*, *Am. J. Dis. Child.*, **43**, 1062 (1932).

[68] Cox, W. M., Jr., and Mueller, A. J., *J. Nut.*, **13**, 249 (1937).

[69] Anderson, H. D., *et al.*, *Am. J. Physiol.*, **129**, 631 (1940).

[70] Peskett, G. R., *Bioc. J.*, **28**, 1657 (1934).

[71] Simms, H. S., Proc. Internat. Dairy Congr., 1931.

[72] Petersen, W. E., *J. Dairy Sci.*, **25**, 71 (1942).

[73] Comparison of the blood and milk sugars of several species.

	Cow	Goat	Sheep	Rabbit	Mare	Sow	Dog	Rat	Woman
Blood sugar (%)	0.05	0.06	0.06	0.12	0.11	0.13	0.08	0.12	0.11
Milk sugar (%)	4.6	4.6	4.5	2.0	7.0	4.0	3.7	3.0	7.0

potassium and phosphate, 4 times as much magnesium, $\frac{1}{2}$ as much protein, $\frac{1}{4}$ as much chlorides, and $\frac{1}{8}$ as much sodium. Some typical milk constituents, such as casein, lactose, and the short-chain fatty acids, are absent in blood.

21.4.1: Osmotic pressure and milk synthesis. In spite of the greater gravimetric concentration of most constituents in milk, the osmotic pressure is the same, about 6.6 atmospheres, in milk and blood, indicating the same total osmotically active molar concentration. How is this sameness of osmotic pressure in milk and blood maintained in the face of the differences in gravimetric composition? Perhaps by the enzymatic change of osmotically active, smaller-molecule transudates derived from blood into osmotically less active, larger-molecule milk constituents. Thus one molecule of milk sugar is derived from two molecules of blood sugar, or from one glucose and two lactic acid molecules, thereby reducing the osmotic pressure in the blood transudate by $\frac{1}{2}$ or $\frac{2}{3}$. Similarly, the amino acids, phosphates, calcium ions, etc., are combined in the secretory cells into larger aggregates—into casein, lactalbumin, and calcium caseinate—resulting in an overall lower osmotic pressure. The osmotic pressure reduction in the transudate in the secretory cells below that of the blood drives the diffusible substances from the blood into the secretory cells as part of the tendency to equalize the hydrostatic or diffusion pressure.

Disturbance of the mammary apparatus, exemplified by mastitis, due to engorgement of the secreting alveoli with fluid as result of cessation of customary milking, affects the selective action of the gland, with a resulting tendency to equalization of milk and blood-serum constituents; this is indicated, for example, by increase in the pH, chloride, catalase, and globulin of milk and decrease in its casein and lactose. Indeed, milk from disturbed glands is detected by its high pH, chloride, and catalase.

The rate of secretion and (to a lesser extent) the composition of milk depend on the pressure within the secretory alveoli. The higher the intra-alveolar pressure, the less the rate of milk secretion and the greater the tendency of the composition of milk to approach that of blood serum. This statement may be illustrated by several dramatically important applications:

(1) When the blood calcium (and sometimes blood sugar) declines below a critical level as result of too rapid lactation (in comparison to the animal's ability to mobilize calcium), the animal develops the typical hypocalcemic and/or hypoglycemic syndrome *milk fever*. Death follows if this is untreated. But if the udder is pumped full of air, both lactation and the drain of blood calcium into the milk are stopped; indeed, some of the calcium in the milk may be turned back to the blood, with the result that the blood calcium (and/or sugar) attains a normal level. Thus, instead of dying, the cow may become normal in a few minutes—an apparent miracle has been performed.

(2) Lactation may be stopped at any time by merely ceasing to milk. The increase in intra-alveolar pressure as a result of failure to remove the milk effectively blocks the lactation process. The applications of this fact are evident: the more frequent and the more complete the milkings, the lower

the average intra-alveolar pressure and the greater the rate of milk secretion; or what is the same, the longer the interval between milkings, the less the milk production per unit time. This is illustrated by the declining curve in Fig. 21.3, prepared from data secured in 1920 or 1921[74].

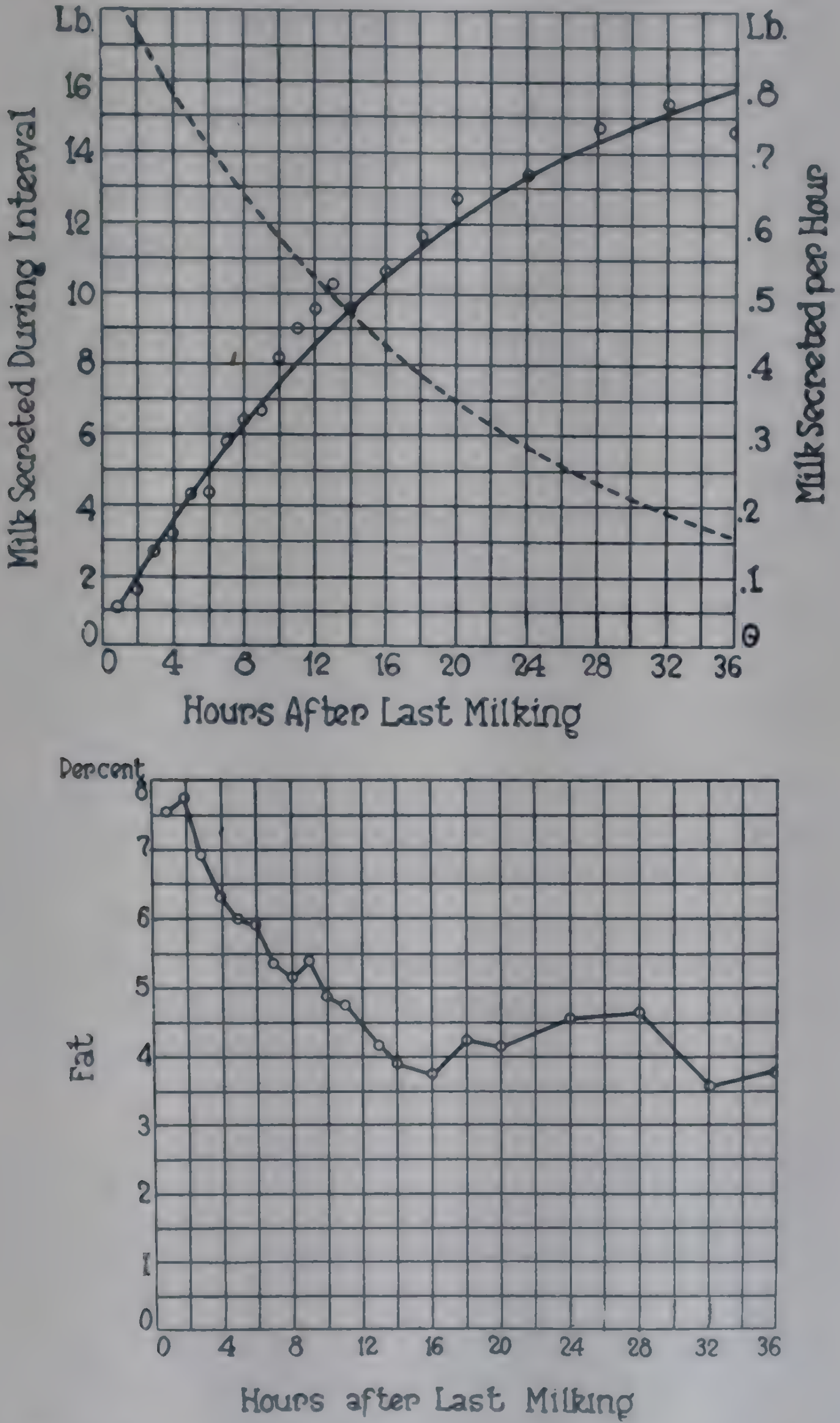

Fig. 21.3. The influence of milking frequency on the rate of milk production.

(3) Unsatisfactory performance, especially rapid "drying up," in some otherwise good dairy cows is explained[75] by the failure of the cow to "let

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[74] Univ. Mo. Agr. Exp. Sta. Res. Bull. 96, 1926, pp. 82. For the more recent literature see Petersen.[72]

[75] Petersen,[72] Turner, C. W., *Hoards Dairyman*, **88**, 685 (1943). Hammond, J., *J. Vet. Rec.*, **16**, 519 (1936).

down" her milk, with resulting continuous high pressure in the alveoli. The "let-down" mechanism is apparently neuro-endocrine in nature. The stimulation (by milking) of the nerve endings in the teat and udder is carried to the central nervous system, which in turn stimulates the posterior pituitary to eject the oxytocic hormone into the blood; the oxytocic hormone stimulates the muscles around the alveoli to contract and thus eject the milk. On the other hand, when the cow is excited, adrenaline production (by the adrenal medulla) is accelerated, thus relaxing the smooth muscles, that is, preventing the muscles around the alveoli from contracting for milk ejection[75, 76].

The involvement of the nervous system is demonstrated by the eventual loss of ability to "let down" the milk following sympathectomy[77] and by similar failure when the animal is frightened or annoyed[76]. Good dairymen, of course, know that it is important to handle cows gently, quietly, and pleasantly (see Sect. 10.8 for a discussion on a broader plane).

The speed of synthesis and diffusion of the various milk constituents is dependent, among other factors, on (1) concentration of milk precursors in the blood, which depends on food supply; (2) concentration of synthetic enzymes in the secretory cells, dependent on the genetic constitution of the animal (although the immediate control of the enzyme concentration may reside in the pituitary or other endocrines, which are directly or indirectly related to the genetic constitution of the animal); (3) intra-alveolar pressure and the factors controlling it.

The concentrations of water, solids, and each of the solid constituents in milk depends on the relative concentrations of each of the various enzymes in the secretory cells. Thus if the concentration of the lactose-synthesizing enzymes is high, relatively more lactose will be produced. Since per unit weight lactose is osmotically more active than fat or protein, the milk will contain more water in order to maintain the osmotic pressure constant. This is probably the reason why the higher lactose concentration in the milk of the horse, ass, and man is associated with higher water content (more dilute[78]).

21.4.2: Colostrum. Colostrum, the mammary secretion in the early stages of lactation, is in some respects intermediate between blood serum and normal milk, especially in being rich in globulin and albumin, poor in potassium and high in sodium, poor in lactose and high in chlorine, as illustrated by Table 21.4, computed by us from Garrett and Overman[79]. The following data on the composition of colostrum during the first four days after calving (Fig. 21.4a) may also be of interest[80].

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[76] Ely, F., and Petersen, W. E., *J. Dairy Sci.*, **24,** 211 and 225 (1941). Swanson, E. W., and Turner, C. W., *Id.*, p. 635. Turner[75].

[77] Cannon, W. B., and Bright, E. M., *Am. J. Physiol.*, **97,** 319 (1931). Bacq, Z. M., *Id.*, **99,** 444 (1932). Selye, H., Collip, J. B., and Thompson, D. L., *Endocrinology*, **18,** 237 (1934), and *Am. J. Physiol.*, **107,** 535 (1934). Simeone, F. A., and Ross, J. F., *Id.*, **122,** 659 (1938).

[78] Blackwood, J. H., and Stirling, J. D., *Bioc. J.*, **26,** 1127 (1932). Grateful acknowledgements are made to W. R. Graham, Jr., for valuable suggestions.

[79] Garrett, O. F., and Overman, O. R., *J. Dairy Sci.*, **23,** 13, (1940).

[80] Ragsdale, A. C. and Brody, S., "The colostrum problem and its solution." *J. Dairy Sci.*, **6,** 137 (1923). Nelson, John B., "Antibody transmission by colostrum." Univ. Mo. Agr. Exp. Sta. Res. Bull. 68, 1924. Brody, S., and Ragsdale, A. C., "Time changes in milk secretion," *Id.*, Res. Bull. 96, 1926, p. 73.

Milking after calving	Milk (lbs)	Solid (%)	Globulin (%)	Casein (%)	Sugar (%)	Fat (%)	Ash (%)
1	10	24	3.3	4.4	2.1	5.3	1.16
2	9	18	1.6	3.4	3.1	4.6	0.95
3	12	14.5	0.90	3.1	3.3	4.4	0.89
4	13	14.4	0.50	2.6	3.5	4.5	0.85
5	16	14.4	0.38	2.6	3.5	4.8	0.82
6	13	14.2	0.33	2.6	3.7	4.6	0.83
7	18	14.2	0.30	2.8	3.9	4.5	0.81
8	17	14.2	0.22	2.3		4.7	0.80

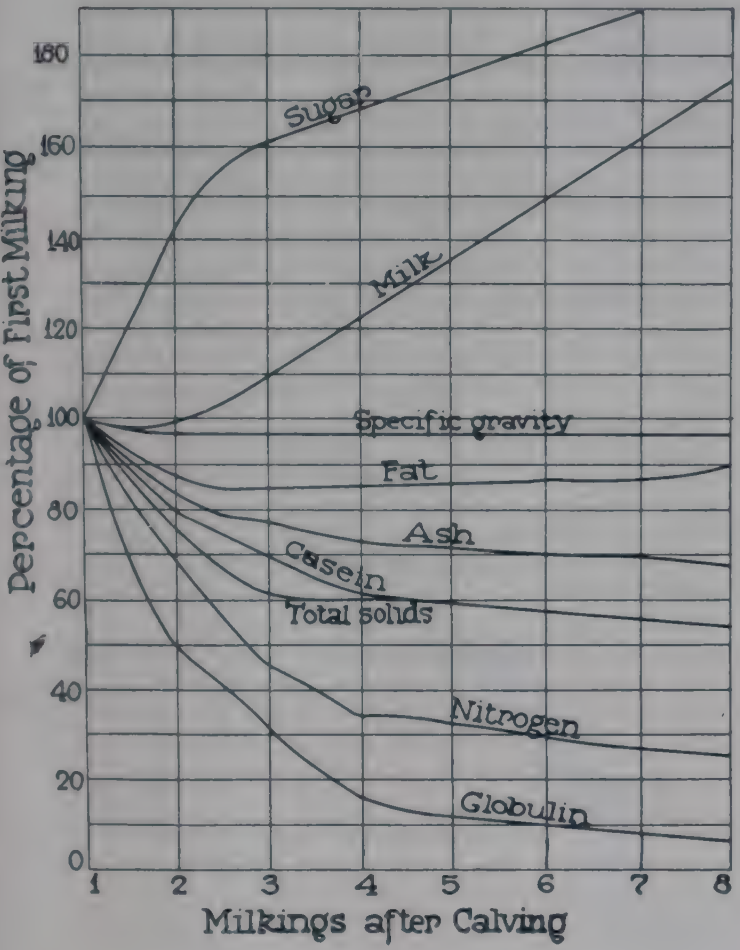

Fig. 21.4a.
Change in composition from colostrum to milk.

In addition to the unusually high level of protein (especially globulin), colostrum is also very rich in vitamin A, perhaps 100-fold that in normal milk, and in other substances, such as immune bodies required by the young until it develops its own immunity[80], and in lysozome[81]. There are also considerable post-colostral changes in the composition of milk, as indicated in Fig. 21.4.

21.4.3: Synthetic powers of the mammary gland. Since, as above explained, milk contains casein, lactose, and short-chain fatty acids not found in blood, and since the general level and proportions of the several constituents in milk are different from those in blood serum, it follows that the mammary gland has synthetic and selective powers. Mammary tissue slices also exhibit synthetic powers *in vitro*. This was demonstrated especially for the synthe-

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[81] Thompson, R., "Lysozome," *Arch. Path.*, **30**, 1096 (1940); Meyer, Carl, *Science*, **99**, 391 (1944); Lawrence, U. L., *Id.*, p. 392.

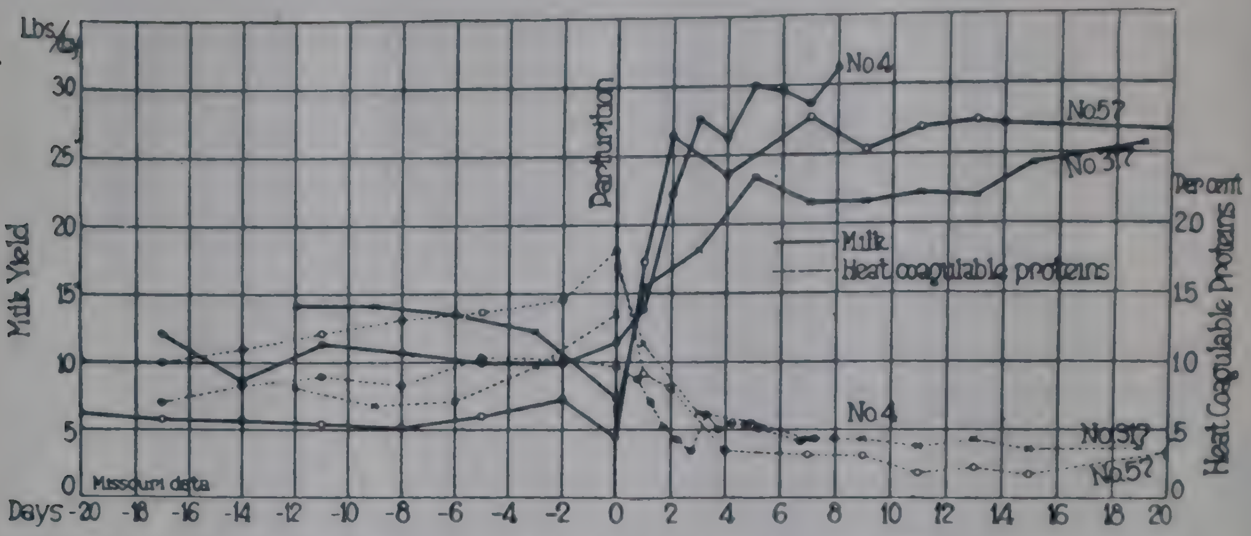

Fig. 21.4b. Changes in milk yield and in heat-coagulable protein with calving.

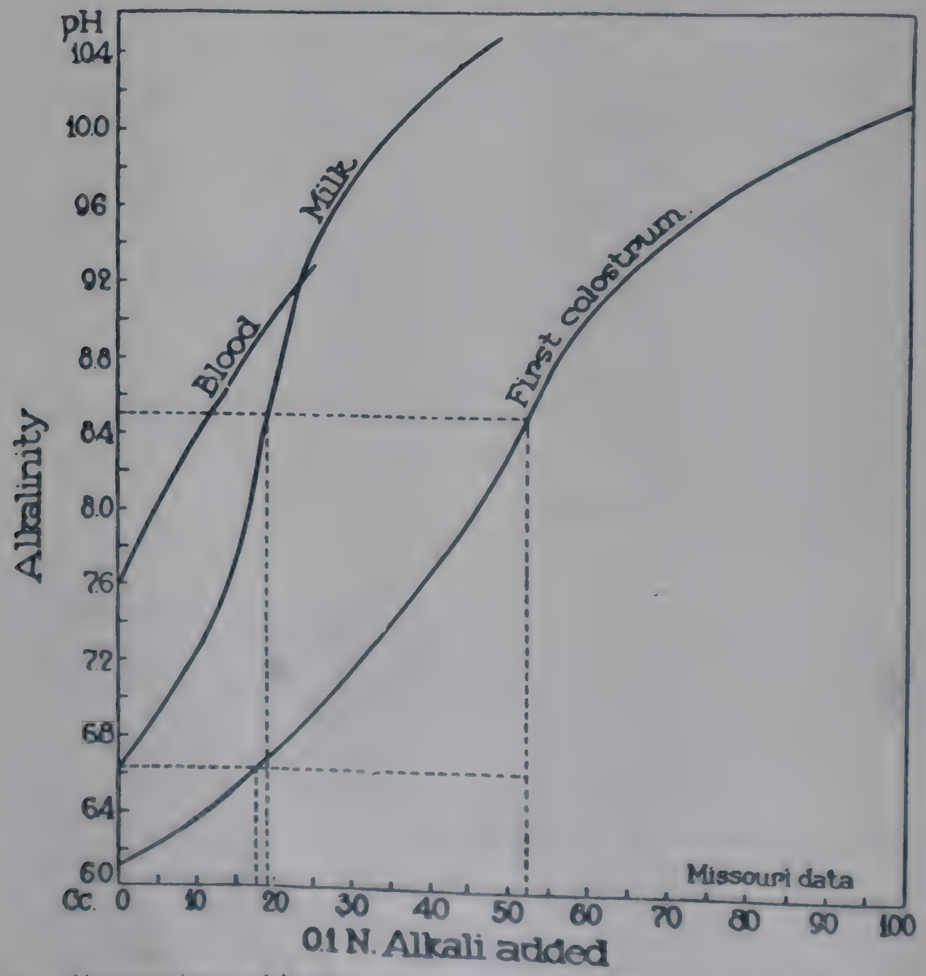

Fig. 21.4c. Comparison of buffer value, or acidity, of milk, colostrum, and blood.

sis of lactose from glucose[82] *in vitro*. It has long been known[83] that there is an arterio-venous difference in the constituents going to make up milk, indicating that the mammary gland takes up the constituents from the blood to make milk. However, the intermediate metabolism, the stages through which the blood constituents pass on their way to milk, is still a virgin field of investigation.

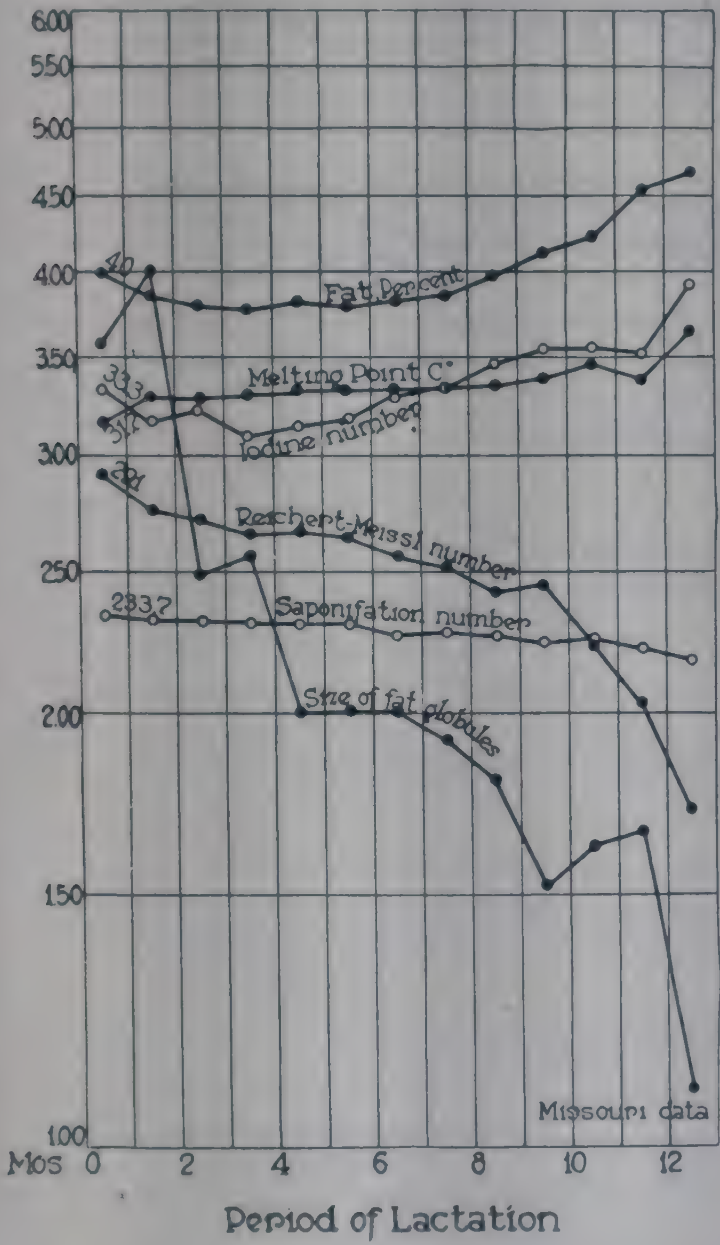

Fig. 21.4d. Change in composition of fat with the advance of the period of lactation. The first numeral on each line represents the corresponding absolute number, e. g., 4.0% fat.

Even the technique of drawing blood for evaluating the uptake of blood constituents for milk production has not yet been worked out satisfactorily. Kaufmann and Magne[83] assumed that the difference in composition between jugular blood and mammary-vein blood represents the uptake by the mammary gland. Blackwood & Stirling[84] criticized this method especially because it overlooks the differences in blood composition resulting from differences in the rate of salivary secretion. Blackwood and Stirling[84] obtained blood simultaneously from the radial artery and mammary vein. Lintzel[85] obtained arterial blood from the heart (left ventricle), Graham from the internal iliac artery through the rectal wall[86], and also by exteriorizing the carotid artery[87]; Maynard[88] obtained blood from the internal pudic artery through the vaginal wall; Petersen[89] analyzed uptake from the blood by perfusion experiments. There are objections to every one of these methods. Excitement of the animal disturbs the normal composi-

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[82] Weinbach, A. P., *Am. J. Physiol.*, **109**, 108 (1934), and *J. Gen. Physiol.*, **19**, 829 (1936). Grant, G. A., *Bioc. J.*, **29**, 1905 (1935). Petersen, W. E., and Shaw, J. C., *Science*, **86**, 398 (1937).

[83] Kaufmann, M., and Magne, H., *C. R. Acad. Sci.*, **143**, 779 (1906).

[84] Blackwood, J. H., and Stirling, J. D., *Bioc. J.*, **26**, 357 and 362 (1932); **28**, 1346 (1934).

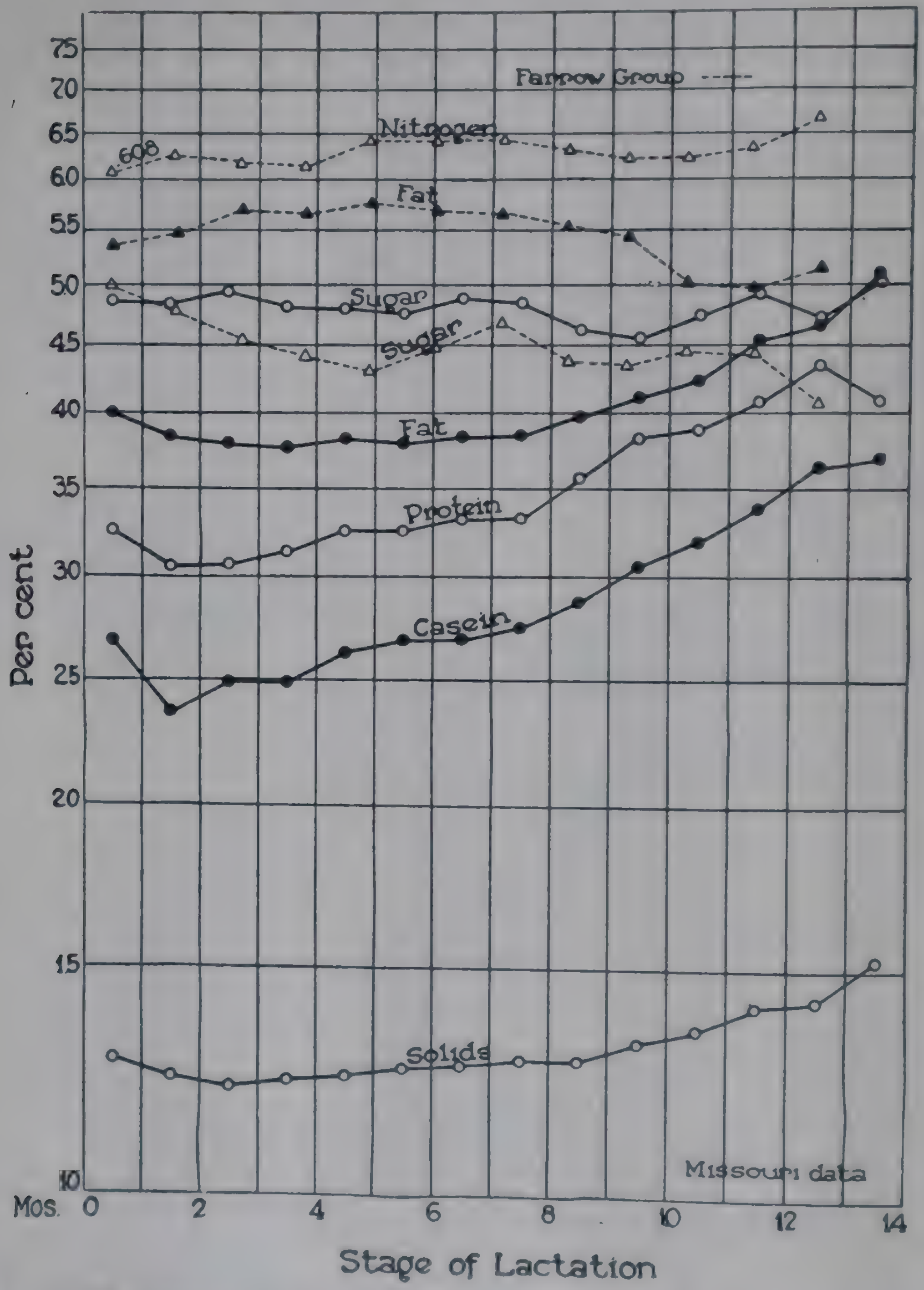

Fig. 21.4e. Changes in the composition of milk with the advance of the period of lactation.

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[85] Lintzel, W., *Z. Zucht.*, **29B**, 219 (1934).

[86] Graham, W. R., Jr., Jones, T. S. G., Kay, H. D., and McIntosh, R. A., *Proc. Roy. Soc.*, **120B**, 319, 330 (1936).

[87] Graham, Turner, C. W., and Gomez, E. T., Univ. Mo. Agr. Exp. Sta. Res. Bull. 260, 1937.

[88] Maynard, L. A., *et al.*, N. Y. Agr. Exp. Sta. Mem. 211, 1938.

[89] Petersen, W. E., *et al.*, *J. Dairy Sci.*, **24**, 139 (1941).

tion of the blood, especially the blood-sugar level. Anesthetizing the animal[90] may overcome this difficulty but introduces others.

To be useful for quantitative interpretation, measurements of arterio-venous difference in blood composition must be accompanied by measurements of the rate of blood flow through the mammary gland. Graham[91] employed the thermostromuhr method[92] for this purpose.

The earlier data of Graham[93] *et al.* and also of Shaw and Petersen[94] (computed on the basis of calcium intake) indicate that about 400 volumes of blood pass through the udder in producing one volume of milk. This means that 20,000 pounds of blood pass through the udder in producing 50 pounds of milk. Graham's thermostromuhr method, however, gave much lower values[95].

21.4.4: Milk-sugar production. Graham reported that milk sugar is derived not only from glucose but also from lactic acid[96] and from blood protein[97]. Some lactose may also be produced from glycoproteins[98].

These results are important because they demonstrate that: (1) blood sugar is not the only source of milk sugar; (2) lactic acid, an important rumen-fermentation product, may participate in and accelerate lactose formation—and, therefore, milk secretion—in ruminants; (3) high dietary protein may stimulate milk secretion; (4) the mammary gland resembles the heart, liver, and other organs in normally utilizing lactic acid for functional activity. It is believed that blood-sugar level is at least one of the major limiting factors in milk secretion; the production of lactose by the mammary gland is believed to control milk volume: 18 lbs of water goes with 1 lb of lactose. Anything which reduces blood sugar (as phlorizin) reduces mostly the milk secretion rate[99] rather than concentration of sugar in milk, although there may also be a reduction in the lactose level of the milk[99, 100]. Alimentary hyperglycemia is, however, without effect; the excess sugar is simply excreted.

21.4.5: Milk-protein production. It is known that there is less nitrogen in mammary-venous than in arterial blood[101]. It is not known, however, to what extent each of the various nitrogen compounds in blood is transformed into the various nitrogen compounds in milk. The difference in amino acids in the arterial and venous bloods is not sufficiently great to account for the milk proteins[102], especially as amino acids are also used in production of lactose. Incidentally, the production of lactose from amino acids, of course, involves deamination and urea production, so that the mammary venous blood contains 3 per cent more urea (1 mg per cent more) than arterial blood. Indeed, the increase in urea nitrogen in the mammary vein may be equivalent to the amino-nitrogen taken up by the gland to produce milk protein[103]. These masking effects and other complications make it difficult to interpret the significance of simple arterio-venous nitrogen differences. It is now believed[89, 90, 91] that blood globulin, including glycoprotein, is taken up by the mammary gland. There are many data which bear on but do not clarify the problem of milk-protein synthesis, such as that there is much more globulin in lactating than in non-lactating gland tissue[104], and that mammary-gland tissue contains considerable arginase[105] (enzyme for splitting urea from arginine).

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[90] Reineke, E. P., *et al.*, *Am. J. Physiol.*, **132**, 535 (1941).

[91] Graham, *J. Biol. Chem.*, **122**, 1 (1937).

[92] Herrick, J. F., and Baldes, E. J., *Physics*, **1**, 407 (1931).

[93] Graham, *et al.*, *Proc. Roy. Soc.*, **120B**, 330 (1936).

[94] Shaw, J. C., and Petersen, W. E., *Am. J. Physiol.*, **123**, 183 (1938).

[95] Computation example: if the arteriovenous difference for calcium is 0.31 mg % and the milk calcium is 120 mg %, the ratio of volume blood flow through the mammary gland to the amount of milk secreted is 120/0.31 = 387. For fat: if the arteriovenous difference, 11.6 mg. % is divided by milk fat content, 400 mg %, it yields a ratio of 344. For lactose: the ratio of milk sugar to blood sugar + lactic acid = 4860/12.4 = 391 volumes of blood to 1 of milk produced. Graham's stromuhr method yielded the ratio 140 to 223 in milking goats and 400 in an almost dry goat.

[96] Graham, W. R., Jr., *J. Biol. Chem.*, **122**, 1 (1937). See also Shaw, J. C., *et al.*, *Proc. Soc. Exp. Biol. and Med.*, **38**, 579 (1938).

[97] Graham, Houchin O. B., and Turner, C. W., *J. Biol. Chem.*, **120**, 29 (1937).

[98] Reineke, E. P., Williamson, M. B., and Turner, C. W., *J. Biol. Chem.*, **138**, 83 (1941).

[99] Gowan, J. W., and Tobey, E. F., *J. Gen. Physiol.*, **15**, 45 and 67 (1931–2). Brown, W. R., Petersen, W. E., and Gortner, *J. Dairy Sci.*, **19**, 147, 177, 243 (1936).

[100] Overman, O. R., and Wright, K. E., *J. Agr. Res.*, **35**, 637 (1929). Petersen, W. E., *et al.*, *J. Am. Vet. Med. Assn.*, **79**, 217 (1931).

[101] Cary, C. A., *J. Biol. Chem.*, **43**, 477 (1920). Blackwood, J. H., *Bioc. J.*, **26**, 772 (1932).

Summing up, Graham *et al.*[106] seem to have demonstrated that only about 40 per cent of the milk protein is derived from blood-serum amino acids, the remainder comes from blood-serum globulins and unidentified nitrogen compounds. This result was confirmed by Shaw and Petersen[107], and others[108].

21.4.6: Milk-fat production. Meigs[109] *et al.* reported a jugular-mammary vein difference in lipid phosphorus, and so concluded that milk fat is derived from blood phospholipids. Subsequent investigators[110] however, found no arterio-venous differences in phospholipids, but differences in total fatty acids, and so concluded that milk fat is derived from neutral fat, perhaps almost exclusively from blood fat.

The respiratory quotient is ordinarily a good index of the nature of the metabolites involved in a given transformation (Ch. 12). Thus an R.Q. of 1.0 indicates that carbohydrate is oxidized; and R.Q. above 1.0 indicates that fat is synthesized. R.Q. measurements of the mammary gland at Missouri[111] yielded values considerably above 1.0 (average of 1.36), indicating synthesis of a portion of the milk fat from blood carbohydrate. The R.Q. values ranged[112] from above unity in the lactating mammary gland of goats, to 0.8 in non-lactating, indicating synthesis of milk fat, especially short-chain fatty acid fats, from blood carbohydrate. It is, however, more generally believed[113] that the short-chain fatty acids in milk are derived from long-chain fatty acids, perhaps from breakdown of oleic-acid fats, in blood[114].

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[102] Graham, W. R. Jr., *et al.*, *Am. J. Physiol.*, **122,** 150 (1938) and *J. Biol. Chem.*, **122,** 275 (1938). Reineke, E. P., *et al.*, Univ. Mo. Agr. Exp. Sta. Res. Bull. 296, 1939; *J. Boil. Chem.*, **138,** 83 (1941).

[103] Shaw, J. C., and Petersen, W. E., *Proc. Soc. Exp. Biol. and Med.*, **38,** 632 (1938).

[104] Jackson, S. M., and Gortner, R. A., *J. Biol. Chem.*, **123,** 719 (1938).

[105] Shaw, J. C., and Petersen, W. E., *Proc. Soc. Exp. Biol. and Med.*, **38,** 631 (1938).

[106] Graham, Peterson, V. E., Houchin, and Turner, *J. Biol. Chem.*, **122,** 275 (1938).

[107] Shaw, J. C., and Petersen, W. E., *Proc. Am. Physiol. Soc.*, 59th Meet., p. 183 (1938).

[108] Reineke, E. P., *et al.*, Univ. Mo. Agr. Exp. Sta. Res. Bull. 296, 1939.

[109] Meigs, E. B., Blatherwick, N. R., and Cary, C. A., *J. Biol. Chem.*, **37,** 1 (1919).

[110] Blackwood, J. H., *Bioc. J.*, **28,** 1346 (1934). Lintzel[85], Graham[86], Maynard[88] and *J. Biol. Chem.*, **92,** 263 (1931); Shaw and Petersen[91] and *J. Dairy Sci.*, **23,** 1045 (1940).

[111] Graham, W. R., Jr., Houchin, O. B., Peterson, V. E., and Turner, C. W., *Am. J. Physiol.*, **122,** 150 (1938).

There is a considerable literature on the qualitative influence of the dietary fat on milk fat[116]. Broadly speaking, such characteristics as the iodine number or hardness of the butterfat tend to parallel within certain limits the corresponding characteristics in the dietary fat. One observer reported that 18 per cent of dietary oil was recovered unchanged in the milk[117]. However, most milk fat is synthesized by the mammary gland, since the chemical composition of milk fat as a whole differs from body and food fat. One of the important contemporary problems in lactation research is the elucidation of the paths, time rates, and mechanisms of these and related transformations. The method of tagging dietary constituents with isotopes, such as with deuterium[118], radioactive iodine[119] and sulfur, heavy carbon[120] and nitrogen should prove helpful in tracing dietary carbon, hydrogen, sulfur, and nitrogen to milk carbon, hydrogen, sulfur and nitrogen[121]. The use of isotopically labelled compounds is undoubtedly the next stage in the study of the intermediate metabolism of milk secretion. Unfortunately, this method is not suitable for experiments with ruminants.

21.4.7: Influence of dietary fat level and of fasting on milk and butterfat production. About a century ago Lawes and Gilbert[122] demonstrated massive conversion of dietary carbohydrate into body fat in farm animals, and about a half century ago Jordan and Jenter[123] similarly demonstrated massive conversion of dietary carbohydrate into milk fat in cattle. However, a certain amount of dietary fat is desirable for optimal production of body fat or milk fat. Thus Maynard[124] and associates demonstrated that dairy animals fed a hay-silage-grain ration containing 6 per cent fat produce above those fed a ration containing 0.7 per cent fat; and cows fed a ration containing 5 per cent fat produce above those fed a ration containing 3 per cent fat[125]: "For feeding practice, it is tentatively concluded that a level of 4 per cent fat in a grain mixture, which is fed at the rate of 1 lb for every 3 to 3½ lbs of milk along with an adequate amount of hay and corn silage, may be considered as substantially adequate." More recently Maynard[126] and associates reported that cows fed a ration containing 7 per cent fat produce 4.4 per cent more milk, 2.0 per cent more fat, and 4.1 per cent more FCM (milk reduced to a 4 per cent fat basis) than cows fed a ration containing 3 per cent fat. Feeding grain mixtures ranging from 2.7 to 4.9 per cent fat did not affect the milk or fat yield in milk cows[127]. Most of the literature[128] is not so clear-cut because of complicating experimental factors which are difficult to interpret. For example, the milk yield may be limited by the animal's capacity to handle bulk, and since a fat-rich ration has less bulk per calorie, the animal may be able to consume more available calories in the diet in the high-fat ration than in the more bulky fat-poor ration and, therefore, yield more milk on the high-fat ration. This is evidently not a fat effect but a bulk effect. Replacing the bulky roughage by iso-caloric quantities of fat-poor grain might have a similarly stimulating effect on milk production.

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[112] Reineke, E. P., Stonecipher, W. C., and Turner, C. W., *Am. J. Physiol.* **132,** 535 (1941).

[113] Reineke, *et al.* feel that if the milk fat all comes from blood fat, there should be no decline in short-chain fatty acids during fast when less blood sugar is available for fat formation. Fasting reduces the R.Q. of the lactating mammary gland to 0.8 and also reduces short-chain fatty acids, which accords with the expectation if the short-chain fatty acids are derived from blood lactic acid or glucose.

[114] Bloor[31], Petersen[72], Hilditch, T. P., and Thompson, H. M., *Bioc. J.*, **30,** 677 (1936). Hilditch and Longenecker, H. E., *J. Biol. Chem.*, **122,** 497 (1938).

[116] Eckles, C. H., and Palmer, L. S., "Influence of plane of nutrition on the cow upon the composition and properties of milk and butterfat: Influence of overfeeding." Univ. Mo. Agr. Exp. Sta. Res. Bull. 24, 1916. Influence of underfeeding. *Id.*, Res. Bull. 26, 1916. "Influence of feeding cottonseed products on the composition and properties of butter." *Id.*, Res. Bull. 27, 1916. Bloor[31], Maynard, L. A., *et al.*, *J. Dairy Sci.*, **19,** 49 (1936). Anderson, W. E., and Williamson, H. H., *Physiol. Rev.*, **17,** 335 (1937).

[117] Buschmann, cited by Bloor[31].

[118] Schoenheimer, R., and Rittenberg, D., *Physiol. Rev.*, **20,** 218 (1940).

[119] Aylward, F. X., Blackwood, J. H., and Smith, J. A., *Bioc. J.*, **31,** 130 (1937).

[120] Carson, S. F., *et al.*, *Science*, **92,** 433 (1940).

[121] See also, Schoenheimer, R., "The dynamic state of body constituents," Harvard University Press, 1942. Borsook, H., *et al.*, *Proc. Roy. Soc.*, **118B,** 488 (1935), and *Ann. Rev. Bioc.*, **12,** 183 (1943). For the conversion of amino acids to carbohydrate, see Olsen, N. S., *et al.*, *J. Biol. Chem.* **148,** 611 (1943), and Gurin, S., and Wilson, D. W., *Fed. Proc.*, **1,** 114 (1942).

[122] Lawes, J. B., and Gilbert, J. H., *Trans. Roy. Soc.*, **2,** 493 (1859).

[123] Jordan, W. H., and Jenter, C. G., New York Agr. Exp. Sta. Bull. 132, 1897; Bull. 197, 1901.

The feeding of cod-liver oil lowers the milk fat[129] (the depressing factor was traced to the triglyceride factor, not the non-saponifiable factor[130]) without, however, affecting the blood lipoids.[131]

Broadly speaking, while reducing a dietary or blood constituent below a certain level lowers the milk yield and often lowers the concentration of this constituent in the milk, the opposite effect, namely, raising the dietary or blood constituent above a certain level, is usually without effect on milk yield or milk composition.

For instance, decreasing blood sugar by insulin or phlorizin decreases milk yield; but increasing blood sugar above the normal level does not influence[132]

[124] Maynard, L. A., *et al.*, Cornell Univ. Agr. Exp. Sta. Bull. 543, 1932; 593, 1934.

[125] Maynard, *et al.*, Cornell Univ. Agr. Exp. Sta. Bull. **727**, 1939. Gibson, G., and Huffman, C. F., Mich. Agr. Exp. Sta. Quarterly Bull. 24, 1939.

[126] Maynard, *et al*, Cornell Univ. Agr. Exp. Sta. Bull. 753, 1941.

[127] Monroe, C. F., and Krauss, W. E., Ohio Agr. Exp. Sta. Bull. 644, 1943.

[128] See, for example, Allen, N. N., *J. Dairy Sci.*, **17**, 379 (1934) (feeding fat, especially butterfat, to cows increases the fat percentage in the milk, but only for about a week. Feeding additional fat to cows on a high-fat level does not increase the fat percentage in milk). See also McCandlish, C., and Struthers, J. P., *J. Dairy Res.*, **6**, 303 (1935). Garner, F. H., and Sanders, H. G., *J. Agr. Sci.*, **28**, 35 (1938).

[129] Golding, J., *et al.* [*Bioc. J.*, **20**, 1306 (1926)] discovered a 30% decline in the fat content of the milk on daily feeding over 56 gm cod-liver oil. This was confirmed by many investigators.

[130] McCay, C. M., and Maynard, L. A., *J. Biol. Chem.*, **109**, 29 (1935).

[131] Williams, H. H., and Maynard, L. A., *J. Dairy Sci.*, **17**, 223 (1934).

[132] Petersen, W. E., and Boyd, W. L., *Proc. Soc. Exp. Biol. and Med.*, **37**, 537 (1937).

the lactose per cent in milk or the milk yield. Likewise, decreasing the protein[133] content below about 16 per cent in the ration of milking cows may depress milk yield; but increasing it above this level does not increase milk yield or change the composition. However, some diffusible constituents in milk not synthesized by the mammary gland, such as vitamins A and D, may be increased enormously above the normal level by their dietary or blood increase.

Related to the problem of dietary level is that of fasting on milk production and composition. As expected, continued fasting lowers the milk yield; but unexpectedly, it raises the concentration of most milk constituents (fat, protein, ash, total solids), though it lowers some, especially lactose. Figs. 21.10 and 21.11 indicate how the percentages of the various milk constituents change with advancing fast. The nature of the changes varies with the time of fast, stage of lactation, individuality of the animal, nutritive condition and so on.

These time changes for 6 days (144 hours) in milk yield and composition do not precisely reflect (except possibly in the sugar) the quantitative time changes in the composition of blood, as illustrated by the following data[134] on blood. The important effect of fasting on lactation may be by way of the influence on the lactogenic hormones, which influence has not yet been investigated.

The following comparisons, modified from Smith[135], on a lactating Ayrshire cow indicate a similar lack of correlation between milk and blood composition.

	Blood serum phosphatase units (%)	Milk phosphatase units (%)	Blood Serum Cl (mg %)	Milk Cl (mg %)	N partition in milk as % of total N				Blood Serum Ca (mg %)	Corpuscular volume (%)
					Casein	albumin + globulin	Non-protein	Protein		
Before fast	4.7	35	350	100	78	15.0	6.5	93	10.5	32
5th day fast	3.0	145	347	107	75	17	7.0	93	9.8	40
10th day fast	4.1	141	337	128	74	19	7.0	93	10.2	41

As previously noted, the nature of the diet changes to some extent the composition of the milk fat. The advance of the period of starvation changes the nature of the nutrients available for the mammary gland, and consequently changes to some extent the nature of the milk fat. Thus the iodine values rise (from 37 to 53) and the Reichert-Meissl value declines (from 25 to 9) during fast[136].

Summarizing this section as a whole, milk is produced in the secretory cells of the mammary gland in several steps, first by filtration, then by synthesis of the major transudate constituents into larger molecules, such as lactose, from glucose and from lactic acid. Such synthesis of one large molecule from several smaller ones produces an osmotic-pressure gradient, forcing more blood transudate into the secretory cells. The rate of milk production is dependent on several factors: (1) the rate of synthesis in the secretory cells,

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[133] See, among others, Harrison, E. S., and Savage, E. S., Different planes of protein intake and milk production. N. Y. (Cornell) Agr. Exp. Sta. Bull. 540, 1932, and Bull. 578, 1933.

[134] Aylward, F. X., and Blackwood, J. H., *Bioc. J.*, **30**, 1819 (1936).

[135] Smith, J. A. B., Howat, G. R., and Ray, S. C., *J. Dairy Res.*, **9**, 310 (1938)

[136] Smith, J. A. B., and Dastur, N. N., *Bioc. J.*, **32**, 1868 (1938).

(2) the concentration of milk precursors in the blood, and (3) the rate of blood circulation through the mammary gland. Measurements of mammary arterio-venous differences in blood composition indicate that: (1) milk sugar is normally produced from (a) blood sugar, (b) lactic acid, (c) protein; (2) milk protein is produced from (a) blood amino acid (up to about 40 per cent), (b) blood-serum globulin and unidentified substances; (3) milk fat from (a) blood-serum fat (or equivalent), (b) blood sugar and possibly blood lactic acid and protein.

Reducing blood sugar or other constituents below their normal levels depresses milk production and reduces the percentage of its constituents; but increasing blood sugar or other blood constituents above their normal levels does not usually increase milk production, or the percentage of sugar, fat, or protein in the milk. For instance, adding fat to a cattle ration already containing 4 per cent fat does not appreciably increase the fat percentage in the milk.

Some diffusible substances not synthesized by the mammary gland, such as iodides and some of the vitamins, tend to enter the milk in some proportion to their concentration in the blood. In this way cow's milk may be enriched in these substances by dietary methods, *e.g.*, with vitamins A (from 400 units per quart on winter feed to 2200 on green summer pasture), with vitamin D (from 5 units per quart in winter light to 50 units in summer sunshine and 160 on feeding about 200 gm or ½ lb irradiated yeast per day), or with iodide (Ch. 6); it cannot, however, be enriched appreciably with calcium, iron, copper, or thiamine, (human milk apparently can be enriched with thiamine by dietary means[137]).

The operation of the law of diminishing returns (Ch. 1) relating the concentration of milk and feed constituents may be illustrated by the following values on the relation between vitamin D in milk and feed.

Vitamin D units fed to cows	0	600	1400	40000	60000
Vitamin D units per quart milk	3	5	10	20	30

There are large bodies of data on such relations by the Ohio and Wisconsin workers and others.

21.5: The heat increment of lactation during feeding and fasting. As might reasonably be expected, the lactation process involves an extra energy expense or heat increment above the non-lactating level. The milk precursors are assembled and synthesized into milk; the lactating mammary gland has more physiologically active tissue; the endocrine system (especially thyroid and pituitary) is physiologically more active during lactation; two to three times more food is ingested during lactation (Fig. 14.20c). Each of these processes involves some form of "work" (Chs. 2 to 5), which, of course, takes place at an energy cost. We shall indeed demonstrate that the heat duction during heavy lactation is about 100 per cent above that during non-lactation level in spite of the following conclusion to the opposite: . . lactation does not increase the heat production. This is not strange, ce the arrangement of food materials in the preparation of milk depends on the hydrolytic cleavages and syntheses which involve hardly any thermal ion[138].” This conclusion[138], generally quoted in textbooks, is based on at production under basal conditions, that is heat production during fast,

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[137] Donelson, E. G., and Macy, I. G., *J. Nut.*, 7, 231 (1934).

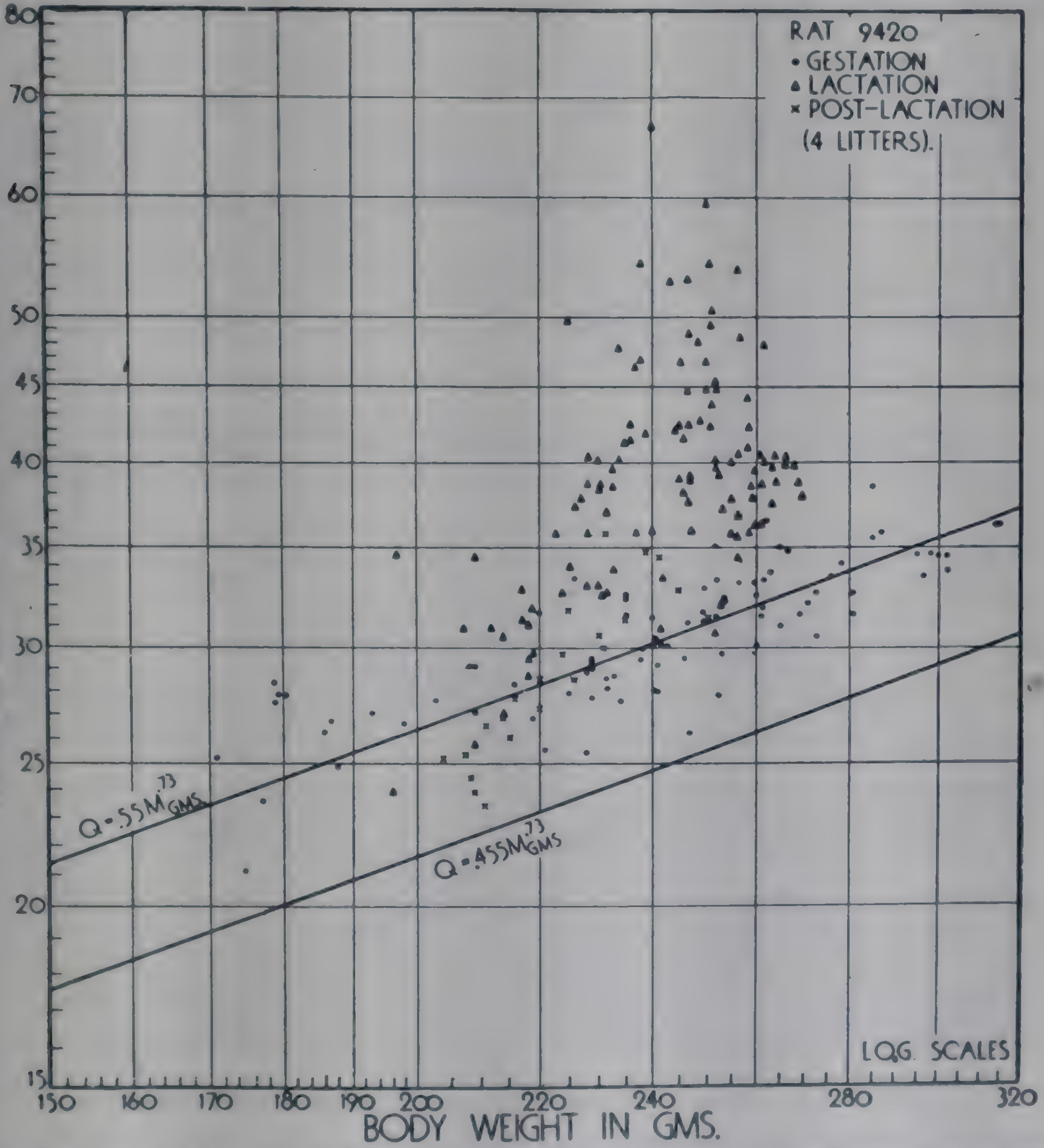

Fig. 21.5a. The influence of lactation on heat production. The smooth lines repre- ct heat production of non-lactating animals (the lower line for mature animals of ferent species, the upper line for rats of different size assuming, the same 0.73 slope the line).

nd we shall show that fasting depresses lactation and heat production. nder ordinary conditions, of course, lactating animals do not fast; indeed, ey consume two or three times as much food as non-lactating animals Fig. 14.20c). As aforenoted, their heat production is perhaps twice as great as that of non-lactating animals, the exact value depending on the lactation level, and therefore food intake. Let us clarify this statement by analyses of data.

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[138] Lusk, G., “The Science of Nutrition,” Philadelphia, 1928.

21.5.1: The heat increment of lactation during normal feeding. Figs. 21.5a to c show[139] that the heat production in lactating rats may be 100 per cent above the non-lactating level. Fig. 21.6 compares similar curves for dairy cattle and rats (assuming that heat production/(weight)$^{0.73}$ is a comparable ratio in cattle and rats). Figs. 21.7a and b show heat production as a function of milk production in rats[140] (taking the litter size in rats as index of milk production) and goats. Whichever representation method is

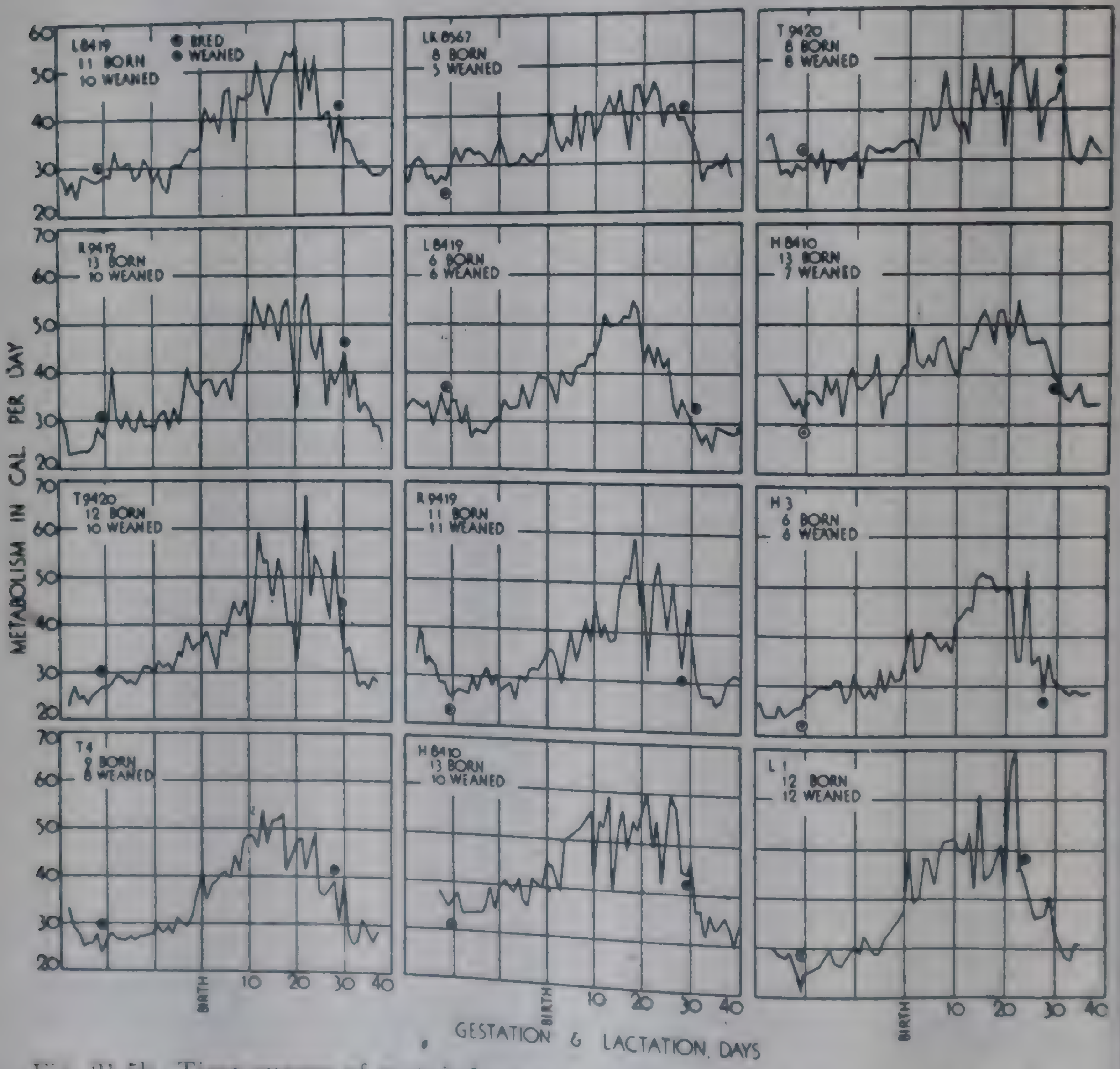

Fig. 21.5b. Time curves of metabolism with the advance of the period of gestation, lactation, and post-lactation rest.

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[139] Brody, S., Riggs, J., Kaufman, K., and Herring, V., "Energy metabolism levels during gestation, lactation, and post-lactation rest," Univ. Mo. Agr. Exp. Sta. Res. Bull. 281, 1938.

[140] Washburn, L. E., Brody, S., and Ragsdale, A. C., "Influence of fasting and re-feeding on milk production," Id., Res. Bull. 295, 1939

employed, the result is the same: heat production in non-fasting animals is proportional to milk production.

The high heat increment of lactation is not due to higher physical activity during lactation because, as shown in Fig. 14.20c, physical activity during lactation is considerably below the non-lactating level. Fig. 14.20c also shows that food consumption during the lactation peak is approximately three times that of the prelactation level. The high lactation heat increment is thus shown to be associated with the high food consumption and milk production rather than with physical activity.

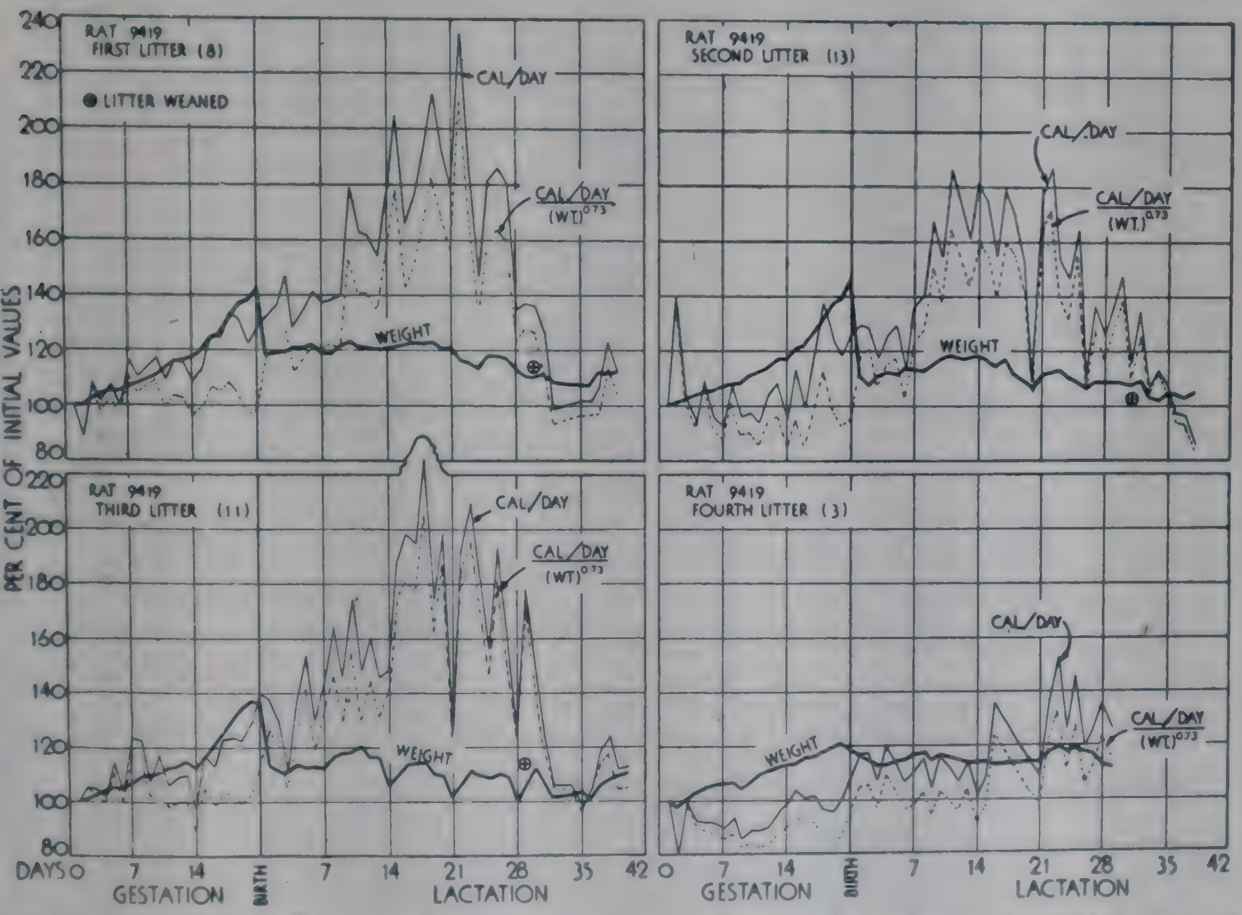

Fig. 21.5c. The relative influence of gestation, lactation, and post-lactation rest on body weight, and heat production per day and per (weight)$^{.73}$ on four successive litters of rat 9419. Note the influence of the number of young on the metabolism level.

21.5.2: The heat increment of lactation during fast. Depending on the rate of milk flow, lactation may treble the food consumption of the non-lactating state (rats[141], women[142], cattle), and it is not surprising that the heat production is also increased. Lusk's conclusion that "lactation does not increase heat production" refers, on the contrary, to a post-absorptive or fasting condition, which tends to depress, perhaps stop, the milk flow. We propose to substantiate the statement that even a relatively short fast virtually stops lactation in the sense of milk yield.

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[141] Slonaker, J. R., *Am. J. Physiol.*, **71**, 362 (1924–5). Wang, G. H., *Id.*, p. 736 (1925), and *Comp. Psychol. Monogr.*, **2**, No. 6 (1923).

[142] Macy, I. G., *et al.*, *J. Nut.*, **4**, 399 (1931).

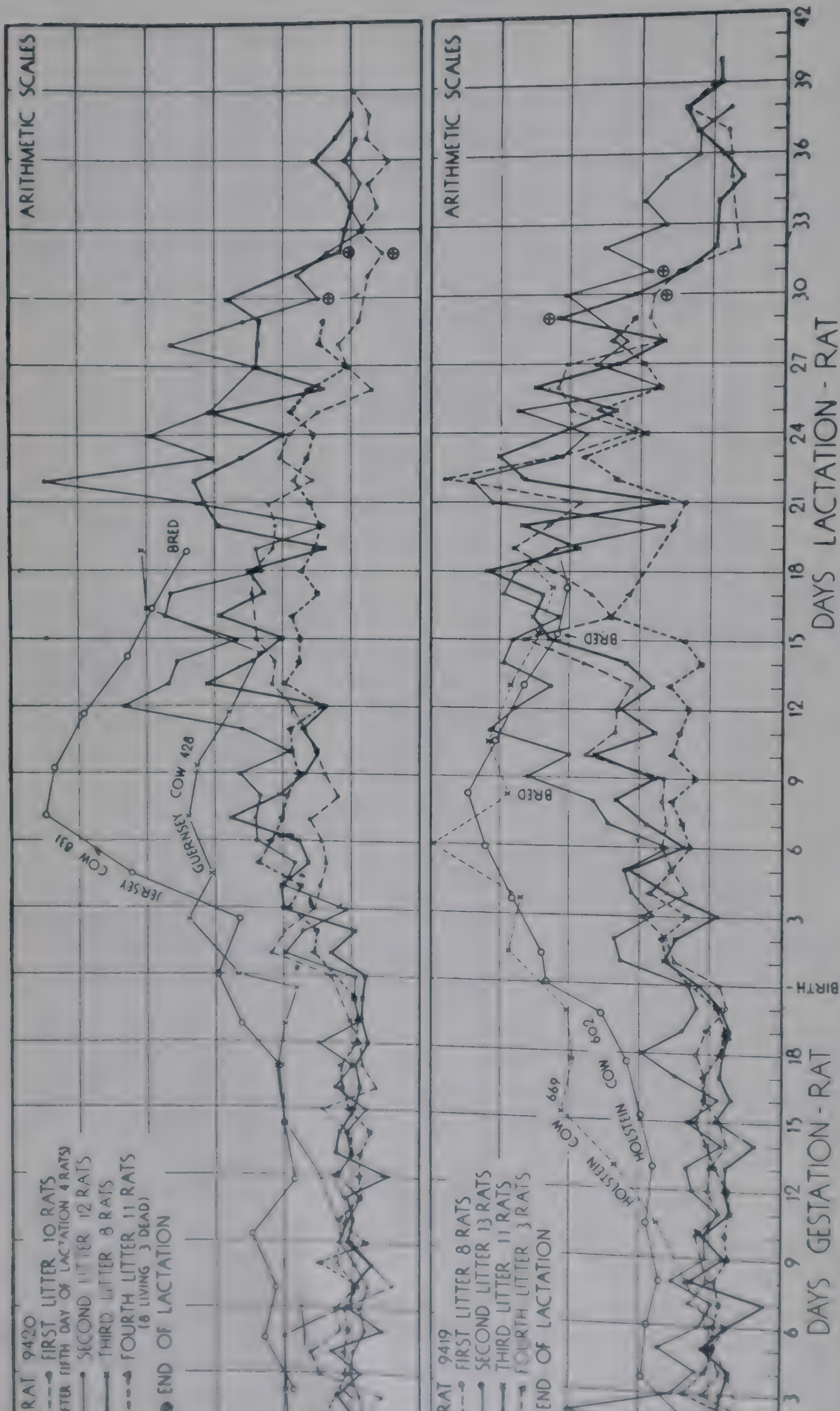

Fig. 21.6. Heat production per weight$^{0.73}$ as function of time during gestation and lactation in cattle and rats, assuming that the ratio $\frac{\text{heat production}}{(\text{weight})^{0.73}}$ is comparable for the two species.

Let us first discuss the influence of fasting on the milk production and heat production in rats[139]. The change in body weight of the 10-day old litter during a 45-minute suckling is taken as index of the litter "food intake", or of the mother rat's milk production.

Fig. 21.8, lower curve, shows that within 10 hours after the food was removed from the cage, the litter "food intake" became zero; that is, the mother's milk production declined to an insignificant level. In the same time, the mother's R.Q. declined from 1.0 or over, to nearly 0.7, indicating that the available carbohydrate in the lactating mother rat disappeared within 10 hours after the food was removed; and the mother's metabolism declined from about 50 to 35 Calories. The baby rats died of starvation within 4 days of the mother rat's fast. Incidentally, this chart shows that milk is not produced at the expense of the mother's stable tissues because the mother fasted 7 days, and recovered on refeeding, while her young died in less than 4 days. If lactation occurred at the expense of the mother's stable tissues, lactation would continue to the end and mother and young would die at approximately the same time. It can thus be concluded that it is true that the

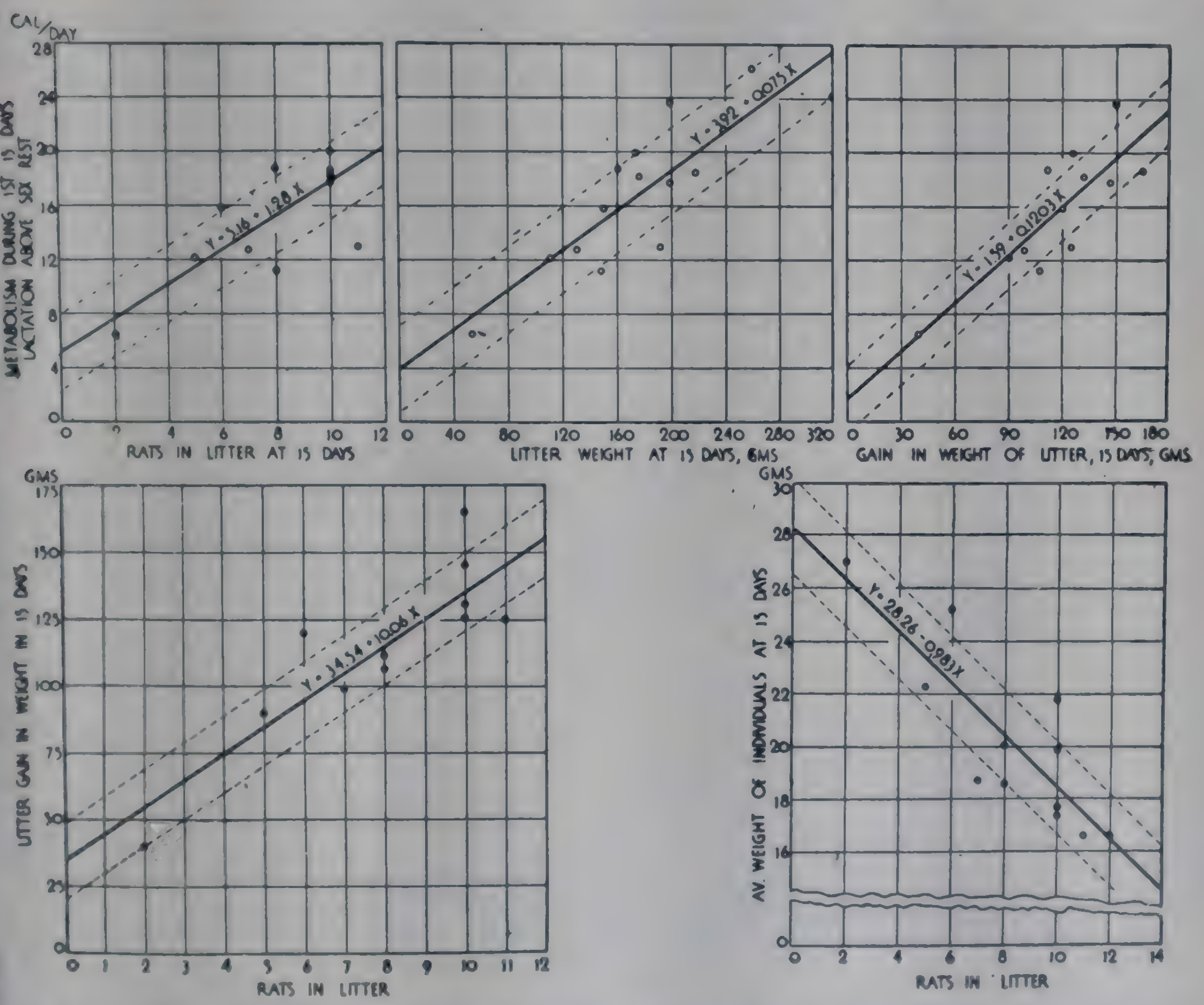

Fig. 21.7a. Heat production as function of litter size and litter-weight gain which, of course, tends to be proportional to milk production of mother rat and related data. The space between the broken lines represents $\frac{2}{3}$ of the data points.

basal metabolism of "lactating" rats is no greater than that of non-lactating because under conditions of basal metabolism there is practically no lactation, and consequently no heat increment of lactation.

Fig. 21.9 shows that the parallelism holds not only for fasting but also for refeeding. Normal milk production almost perfectly parallels feed consumption, heat production, and R.Q.

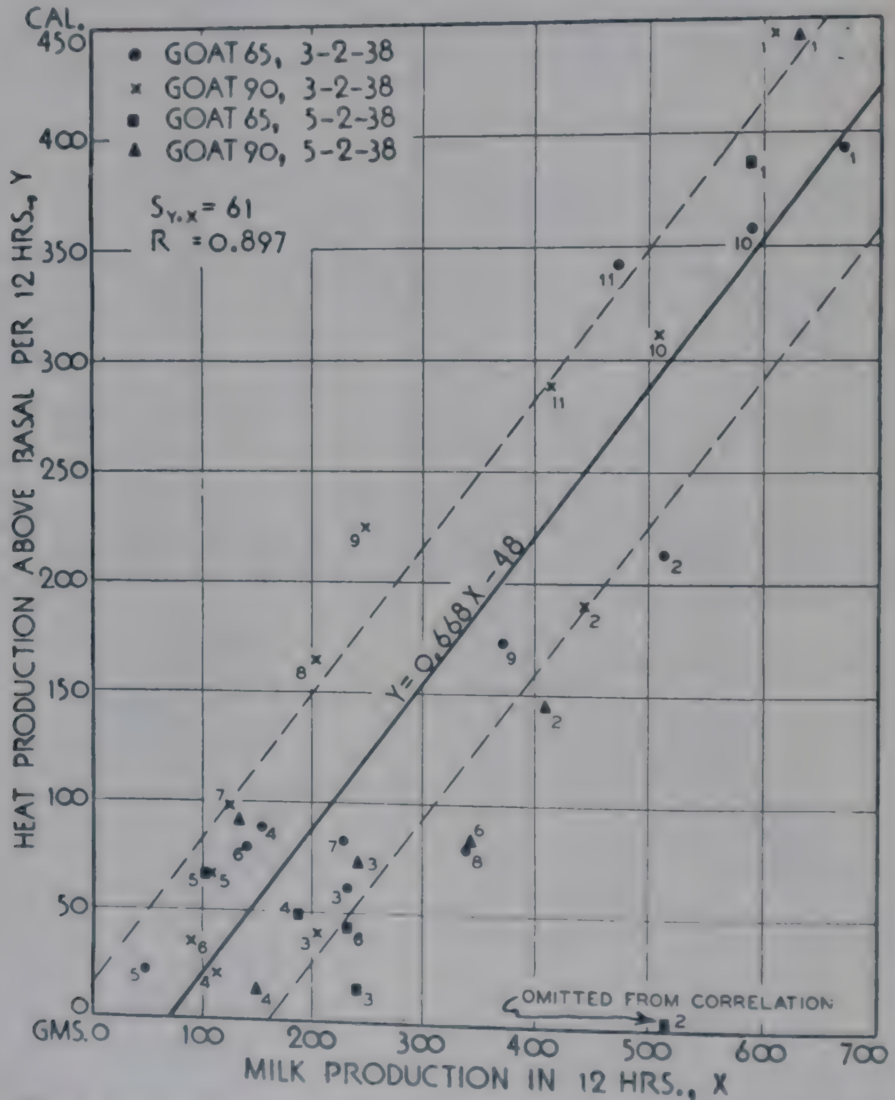

Fig. 21.7b. Heat production per 12-hour period above the basal level plotted against milk production during fast and refeeding of goats. The data points representing successive 12 hour periods are numbered serially. $S_{Y.X}$, the standard error of Y about the equation line (Y as a function of x), has a value of 61, which means that the heat production above basal can be estimated from the equation with the odds 68 out of 100 that the error will not exceed 61 Calories.

Similar results were obtained on goats[143] (Fig. 21.10) and cattle[143] (Fig. 21.11).

Although we have no data on the influence of fasting and refeeding on milk secretion and heat production in women, data on rats, goats, and cattle demonstrate that milk production, heat production, and respiratory quotient fall and rise in percentage parallel with fasting and refeeding. Hence the conclusion that there is a large heat increment and energy cost of lactation. Lactation is said to begin in the later half of gestation; lactation is an outgrowth of gestation (Sect. 7.2). The problem of prenatal growth and metabolism during gestation was previously discussed (Sect. 14.7, see Figs. 14.17 to 14.23).

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[143] Washburn, Brody, and Ragsdale. The curves for the goats were plotted from original data; the curves for the cattle were plotted from data by Overman, O. R., and Wright, K. E. *J. Ag. Res.*, 35, 637 (1927).

21.6: Energetic efficiency of milk production. The overall economy of milk production is composed of many elements, the two outstanding of which are (1) energetic efficiency of the lactation process discussed in this section; (2) size of animal, "dairy merit", and plane of nutrition discussed in the following chapter.

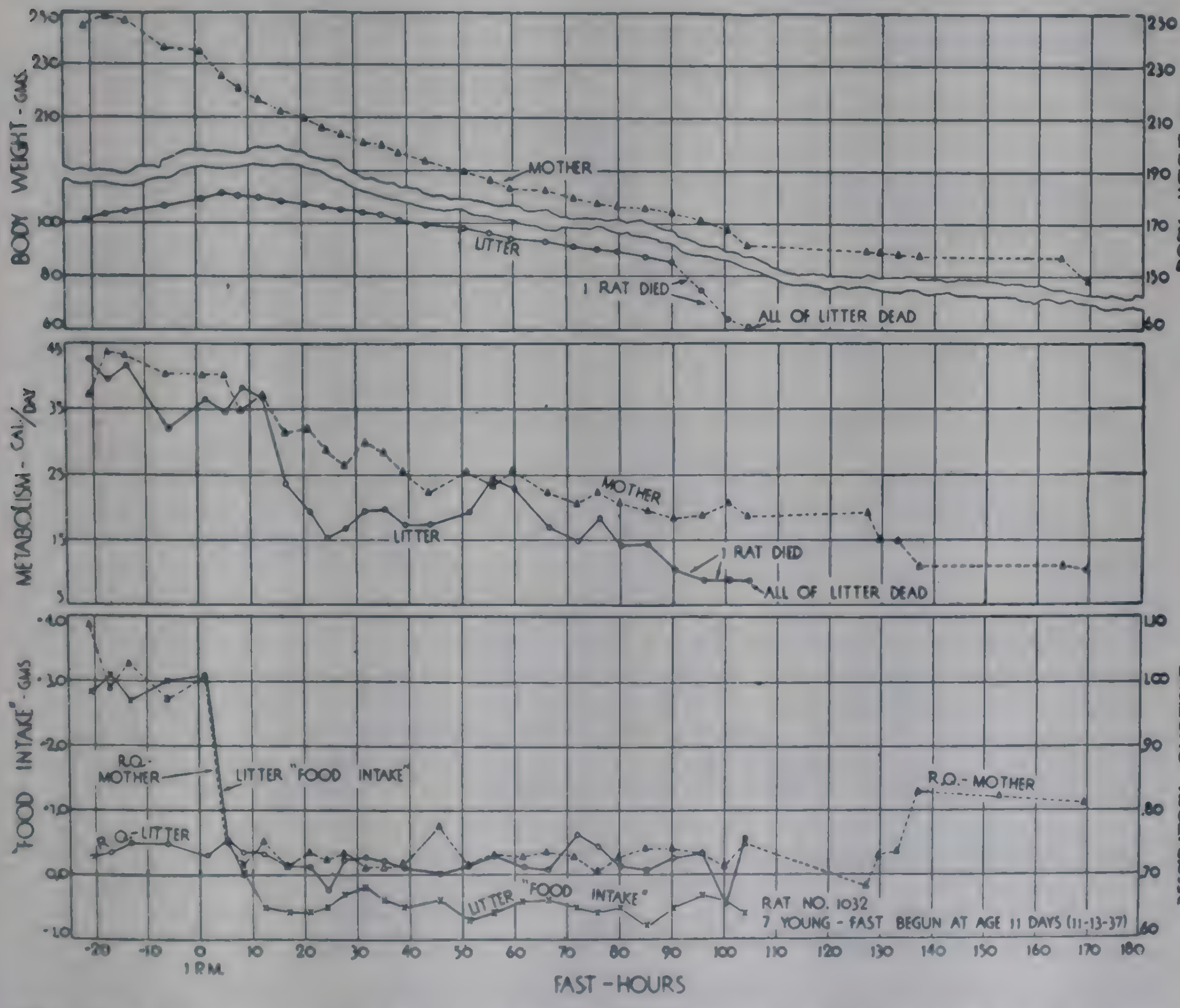

Fig. 21.8. The course of: heat production (Cal/day and Cal/kg/day), R.Q. (respiratory quotient) and litter "food intake", with time after feeding of the mother. Note the parallelism between the R.Q. of the mother and the "food intake" of the litter. Note that the gain in weight of the litter during 45-minute suckling declined from three gm. to zero within eight hours after the food was removed.

As defined elsewhere (Chs. 1 and 22), *gross* energetic efficiency of milk production is the ratio of milk calories produced to feed calories consumed, *including maintenance cost*; *net* energetic efficiency is the ratio of milk calories to feed calories *above the maintenance cost.*

$$\text{Gross efficiency of milk production} = \frac{\text{milk calories produced}}{\text{feed } (TDN) \text{ calories consumed including maintenance cost}} \qquad (21.1$$

$$\text{Net efficiency of milk production} = \frac{\text{milk calories produced}}{\text{feed } (TDN) \text{ calories consumed above the maintenance cost}} \qquad (21.2$$

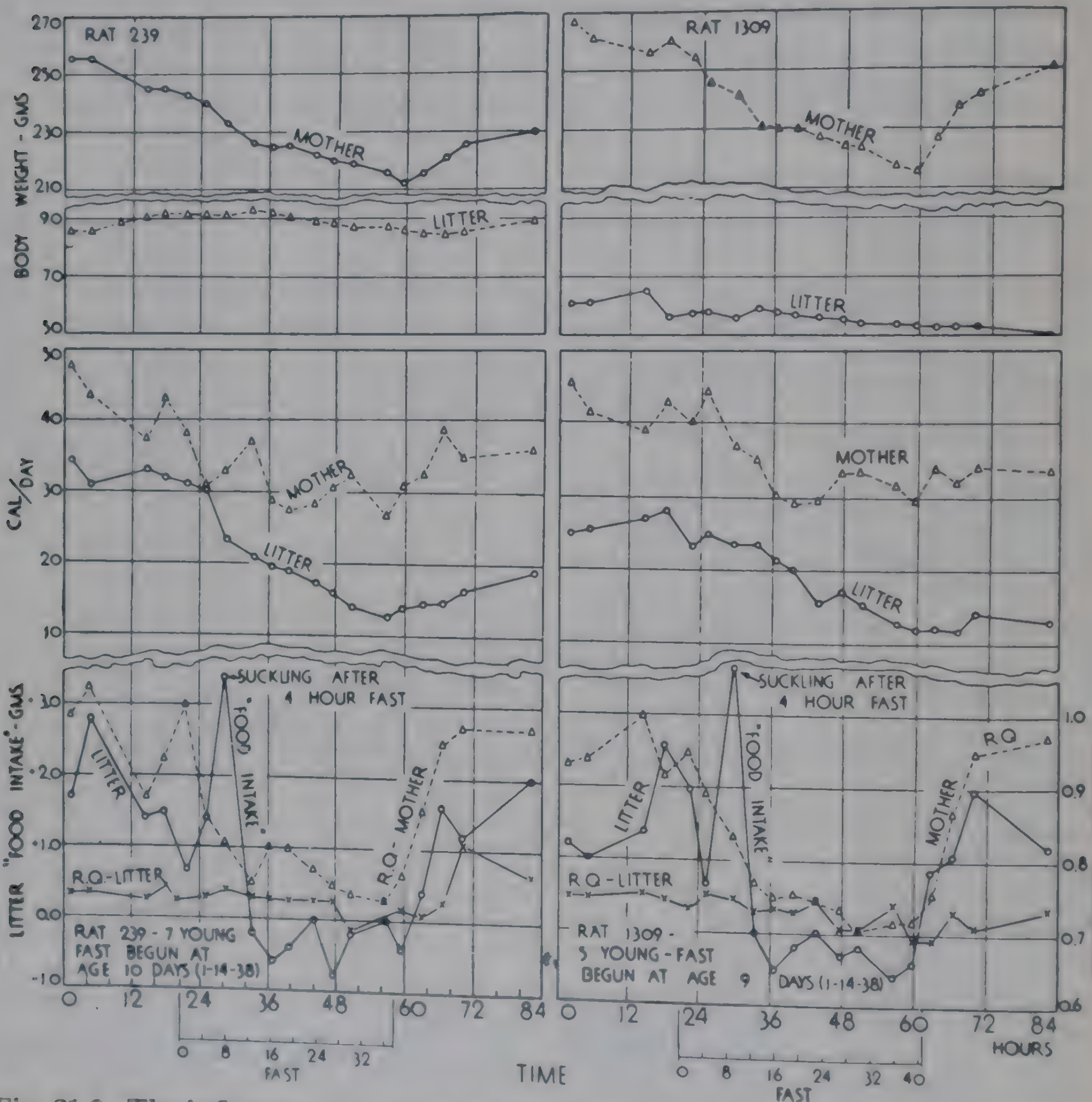

Fig. 21.9. The influence of fasting and refeeding of mother rat on her milk productio (measured by litter-weight gain during suckling), metabolism, body weight, and R.Q Note the prompt decline in "litter food intake" and metabolism on fasting and rise o refeeding.

If body weight is unchanged during lactation, the *gross* efficiency is com puted by replacing the numerator in equation (21.1) by the milk energy, ac cording to the method of Gaines[144] (convert milk to FCM from Table 22 and multiply FCM pounds by 340, the caloric equivalent per pound FCM) and by replacing the denominator by the TDN energy consumed (multip pounds TDN by 1814, the assumed caloric equivalent per pound TDN Equation (21.1) then becomes:

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[144] Gaines, see Table 22.3.

$$\text{Gross efficiency of milk production} = \frac{340 \times FCM \text{ (lbs)}}{1814 \times TDN \text{ (lbs)}} \qquad (21.3)$$

In addition to the overall gross and net efficiency categories as defined above, one may measure the efficiencies of the various component processes as, for example, the energetic efficiency of the mammary gland alone in assembling the milk precursors in the blood and synthesizing them into milk.

Graham[102] and associates at the Missouri Station indeed computed the mammary-gland energetic efficiency from the arterio-venous differences in oxygen and carbon dioxide content. They reported that the gross efficiency of the mammary gland, including its maintenance cost, is approximately 90 per cent; that is, 10 per cent of the milk-precursor energy entering the mammary gland was expended for the synthesis of milk from its precursors, and for the maintenance of the gland[145]. Thus, for example, if an 1100-lb cow

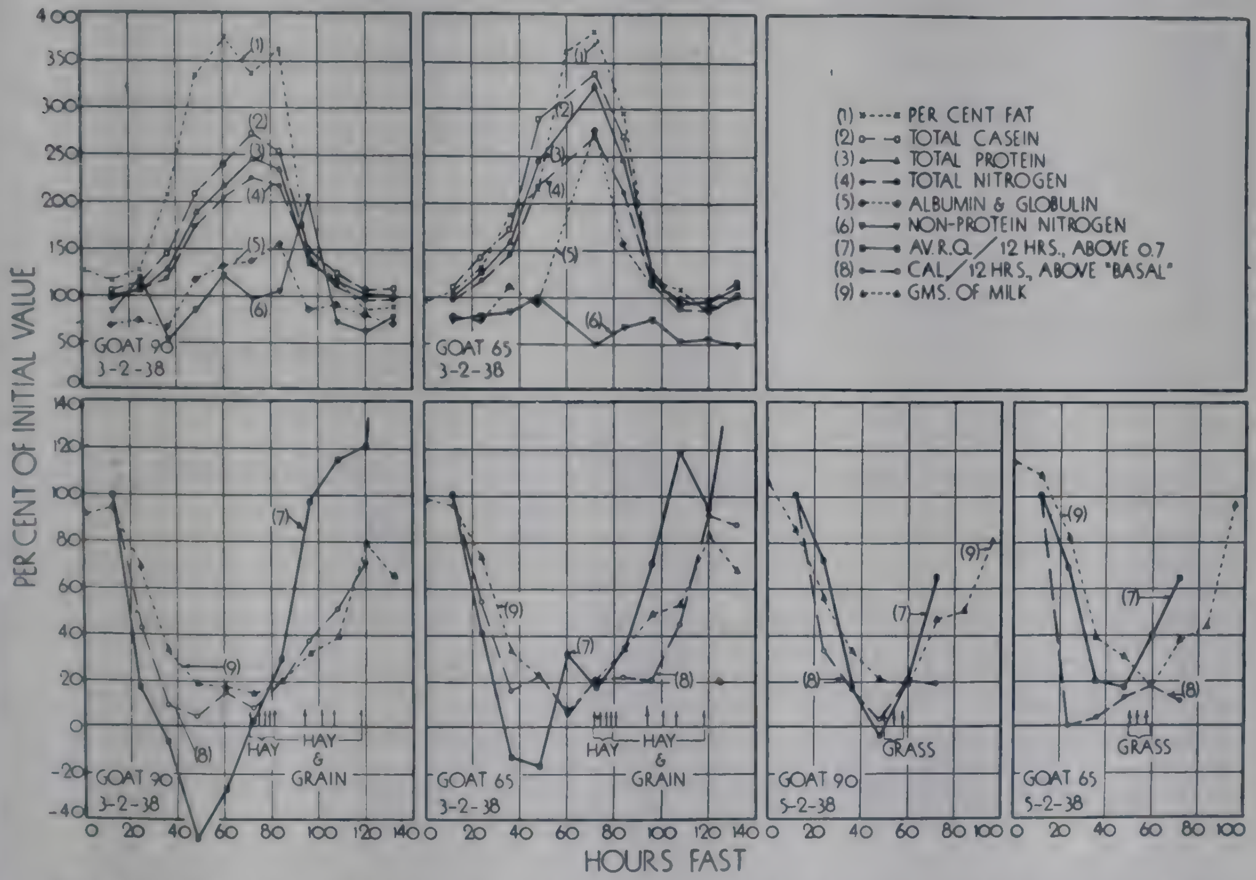

Fig. 21.10. The lower half represents comparison of the time curves of milk production (curve 9), heat production above base (curve 8), and R.Q. above 0.7 (curve 9), all in terms of percentage of normal initial values. Note the striking parallelism of these curves for goats and compare to the parallelism of the curves in Fig. 8 for rats. The upper curve represents the time changes in composition of the milk with advancing fast and refeeding.

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[145] The efficiency was computed from the ratio:

$$\frac{\text{Milk energy per cc milk}}{\frac{\text{Blood flow} \times 100}{\text{milk yield}} \times 1.09\,(\text{CO}_2 \text{ vol.\%} - \text{O}_2 \text{ vol.\%}) + 5.01\,(\text{O}_2 \text{ vol \%}) + \text{milk energy/cc milk}}$$

The ratio of blood flow through the mammary gland to milk produced ranged from 150:1 to 250:1; arterial O_2, 12.87 mg %; mammary vein O_2, 7.53%; O_2 decrement, 5.34 mg.%; arterial CO_2 increment, 6.86%; R.Q., 1.3; milk energy, 80.65 Cal per 100 cc produces 40 lbs FCM or 13600 Cal of milk, 10 per cent of this value, that is 1360 Cal of energy is wasted, *i.e.*, given off as a heat increment of mammary-gland activity. Incidentally, since the "basal metabolism" of a 1100-lb cow is about 7000 Cal, the 1360 Cal heat increment of mammary-gland activity constitutes nearly 20 per cent of the basal metabolism. It was noted in the previous section that the heat increment of heavily lactating animals is about 100 per cent above that of the non-lactating level.

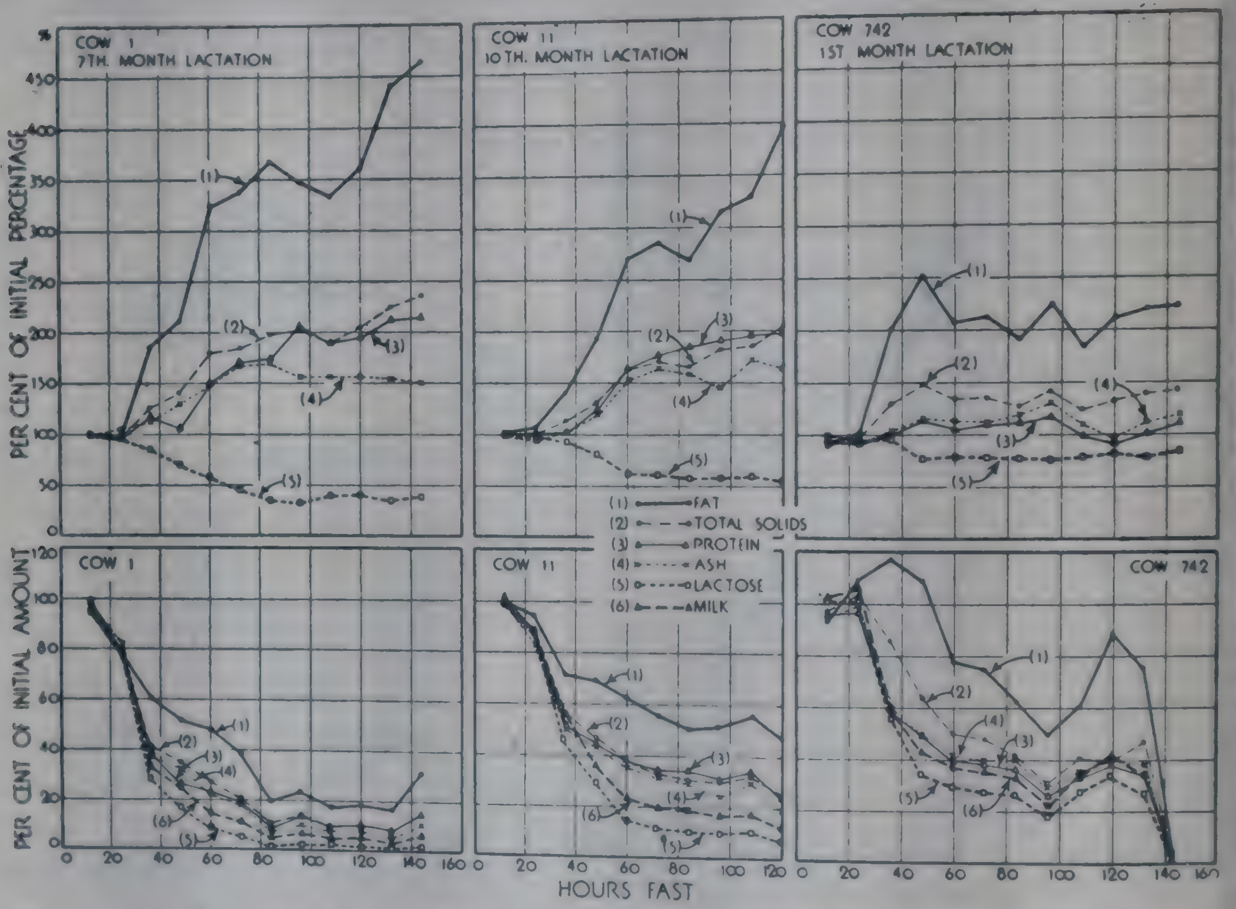

Fig. 21.11. Fasting dairy cows for 3 days (said to be the time required to attain the post-absorptive level for "basal metabolism" in cattle) reduces milk yield to 5–20 per cent of the original level (depending on the stage of lactation and individuality of the cow). This result substantiates the conclusion based on the rat and goat data that it is not possible to measure the basal metabolism of animals yielding *normal* amounts of milk because the fast required for *basal* metabolism profoundly depresses milk production. The upper curves represent changes in percentage composition of milk; the lower curves, changes in absolute yield; both upper and lower curves are represented in terms of percentages of the initial values. From the upper curves, note that fasting, which reduces milk yield increases fat percentage (1) but reduces lactose percentage (5).

21.6.1: Gross efficiency of milk production in dairy cattle. Using equation (21.3) above, we[146] computed, first, the gross efficiency of milk production of 368 dairy cows (data in Table 21.7) with the results summarized in Table 21.6. These tables show that the given cows—weighing from 1000 to 1300 pounds, producing 28 to 50 lbs FCM and consuming 17 to 28 lbs TDN per day—pro duced milk at a gross energetic efficiency of 28 to 34 per cent; that is, 28 to 34 Cal milk were produced per 100 Cal TDN consumed. In other words, about $\frac{1}{3}$ of TDN energy consumed by the superior cows was recovered in the milk; or the TDN energy consumed was about 3 times the FCM energy produced.

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[146] Brody, S., and Procter, R. C., "Energetic efficiency of milk production and the influence of body weight thereon," Univ. Mo. Agr. Exp. Sta. Res. Bull. 222, 1935. Brody, S., and Cunningham, R., *Id.* Res. Bull. 238, 1936.

Additional significant features of this table: (1) the daily FCM production was 10,000 to 17,000 Cal per day and TDN consumption 32,000 to 50,000 Cal per day; (2) the milk calories produced were from $1\frac{1}{2}$ to 2 times the estimated basal metabolism of the cows; (3) depending on the milk yield and efficiency, from $\frac{1}{3}$ to $\frac{1}{2}$ of the total TDN consumed was used for maintenance, leaving from $\frac{1}{2}$ to $\frac{2}{3}$ for milk production; (4) the cows consumed 2 to 3 times as much TDN during lactation as during non-lactating maintenance, a result in good agreement with the one previously cited for lactating rats and also for high-milking women.

The highest energetic efficiency of milk production that we encountered (estimated from the nomograph, Fig. 22.2) was 47.5 per cent for the Jersey champion cow Stonehurst Patrician's Lily, a 700-pound cow which produced 25,946 lbs FCM for the year Much higher absolute production records were made, but at lower energetic efficiencies. Thus the U. S. Holstein champion cow Carnation Ormsby Butter King "Daisy" produced[147] 36,476 lbs FCM per year, which is 40.5 per cent $\left(= \frac{36{,}476 - 25{,}946}{25{,}946} \times 100\right)$ above that of the Jersey champion production; but since the Holstein cow weighed 1700 pounds, which is 143 per cent $\left(\frac{1700\text{–}700}{700} \times 100\right)$ above that of the Jersey weight, and since the Holstein cow probably used about 91 per cent $\left(= \frac{12.09 - 6.33}{6.33} \times 100\right)$ more TDN for maintenance than the Jersey, the gross energetic efficiency of milk production of the Holstein was computed (from Fig. 22.2) to be only 43.5 per cent in contrast to gross efficiency of the Jersey of 47.5 per cent. This 47.5 per cent gross efficiency value with regard to TDN is probably near the limit of biological possibility. The detailed production records of "Daisy" are given in the following table.

Production Records of Carnation's "Daisy"

Lactation month	FCM (4% milk), lbs./day	FCM, Calories/day	Estimated gross energetic efficiency
1	97.38	33109	43.8
2	105.61	35907	44.6
3	103.16	35074	44.4
4	110.51	37573	45.3
5	107.68	36611	44.9
6	102.85	34969	44.3
7	102.94	35000	44.3
8	97.15	33031	43.7
9	96.31	32745	43.6
10	91.89	31243	42.9
11	90.01	30603	42.7
12	91.18	31001	42.9

It is significant that the gross energetic efficiency of milk production of "good" dairy cows is of the same order as the gross efficiency of early postnatal growth on "good" diets, namely about 30 per cent (Ch. 3). Thus chicks and cattle grow at, roughly, the same gross energetic efficiency in early postnatal life, just as large and small cows tend to produce milk with equal gross energetic efficiency.

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[147] See *Holstein-Friesian World*, Feb. 22, 1936.

It will be presently shown that the *net* energetic efficiency of milk production with respect to TDN consumption in dairy cattle is of the order of 60 per cent. Since *net* efficiency does not include maintenance cost, therefore *gross* efficiency, which does include maintenance cost, can never reach the net-efficiency of 60 per cent level; 50% is probably as high a gross efficiency level with respect to TDN consumption as it is possible to achieve.

21.6.2: Gross efficiency of milk production in dairy goats. The efficiencies of seven goats were investigated[148]. Their weights averaged 42.5 kg (93.5 lbs); daily milk production 2114 Cal, or 6.2 lbs FCM; gross efficiency of milk production with respect to TDN ranged from 32 to 40 per cent, averaging 34.9 per cent. The conclusion follows that the gross energetic efficiency of milk production in dairy goats is of the same order as that of dairy cattle.

It is significant that women, in the same weight class with goats, produce milk at the same level and at the same gross efficiency as goats. Thus wet nurses were reported to produce 4.5 liters (about 10 lbs) per day[149], and 3.1 liters (near 7 lb or 2100 Cal) milk per day[150]. These women[150] converted 30 to 50 per cent of the food calories to milk calories, confirming Hoobler[151], who observed women converting from 41 to 47 per cent of their dietary calories into milk, that is, producing milk at a gross energetic efficiency of 41 to 47 per cent.

21.6.3: Gross efficiency of milk production in rats. There is some difficulty in obtaining the milk-energy production in rats. However, we[152] are confident of the following results because they represent concordant values obtained by two methods as follows:

(A) The milk produced in the rat was estimated from the weight gains of the litter during timed suckling intervals, corrected for weight losses due to urination, defecation, and insensible perspiration:

$$\begin{array}{l}\text{Gross efficiency}\\ \text{of milk produc-}\\ \text{tion in the rat}\end{array} = \frac{\begin{array}{l}\text{Gain in litter weight (gm) during}\\ \text{suckling plus loss in litter weight}\\ \text{due to insensible perspiration}\end{array} \times \begin{array}{l}\text{Calories}\\ \text{per gm}\\ \text{rat milk}\end{array}}{\text{Calories } TDN \text{ consumed by mother}} \qquad \text{(A)}$$

The caloric value of rat milk was estimated from its composition. We assumed, on the basis of data by Mayer[153], and by Cox[154], that rat milk contains 16 per cent fat, 12 per cent protein, 3 per cent carbohydrate; therefore, a gram of rat milk has a combustion value of 2.3 Cal ($9.5 \times 0.16 + 5.6 \times 0.12 + 0.03 \times 4 = 2.3$).

(B) The milk produced in the rats was also estimated from the energy stored in the litter, plus maintenance of the litter.

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[148] Brody, S., Sandburg, Mrs. Carl, and Asdell, S. A., "Growth, milk production, energy metabolism and energetic efficiency of milk production in goats." Univ. Mo. Agr. Exp. Sta. Res. Bull. 291, 1938.

[149] Ylinen, L., *Acta. Paediat.*, **21**, 473 (1937). Macy, I. G., *J. Dis. Child.*, **39**, 1186 (1930).

[150] Shukers, C. F., *et al.*, *J. Nut.*, **5**, 127 (1932).

[151] Hoobler, B. R., *Am. J. Dis. Child.* **14**, 105 (1917); *Jour. Am. Med. Assn.*, **69**, 42 (1917).

[152] Brody, S., Nisbet, R. N., "A comparison of the amounts and energetic efficiencies of milk production in rat and dairy cow." Univ. Mo. Agr. Exp. Sta. Res. Bull. 285, 1938.

[153] Mayer, D. T., *J. Nut.*, **10**, 343 (1935).

[154] Cox, W. M. Jr., and Mueller, A. J., *J. Nut.*, **13**, 249 (1937).

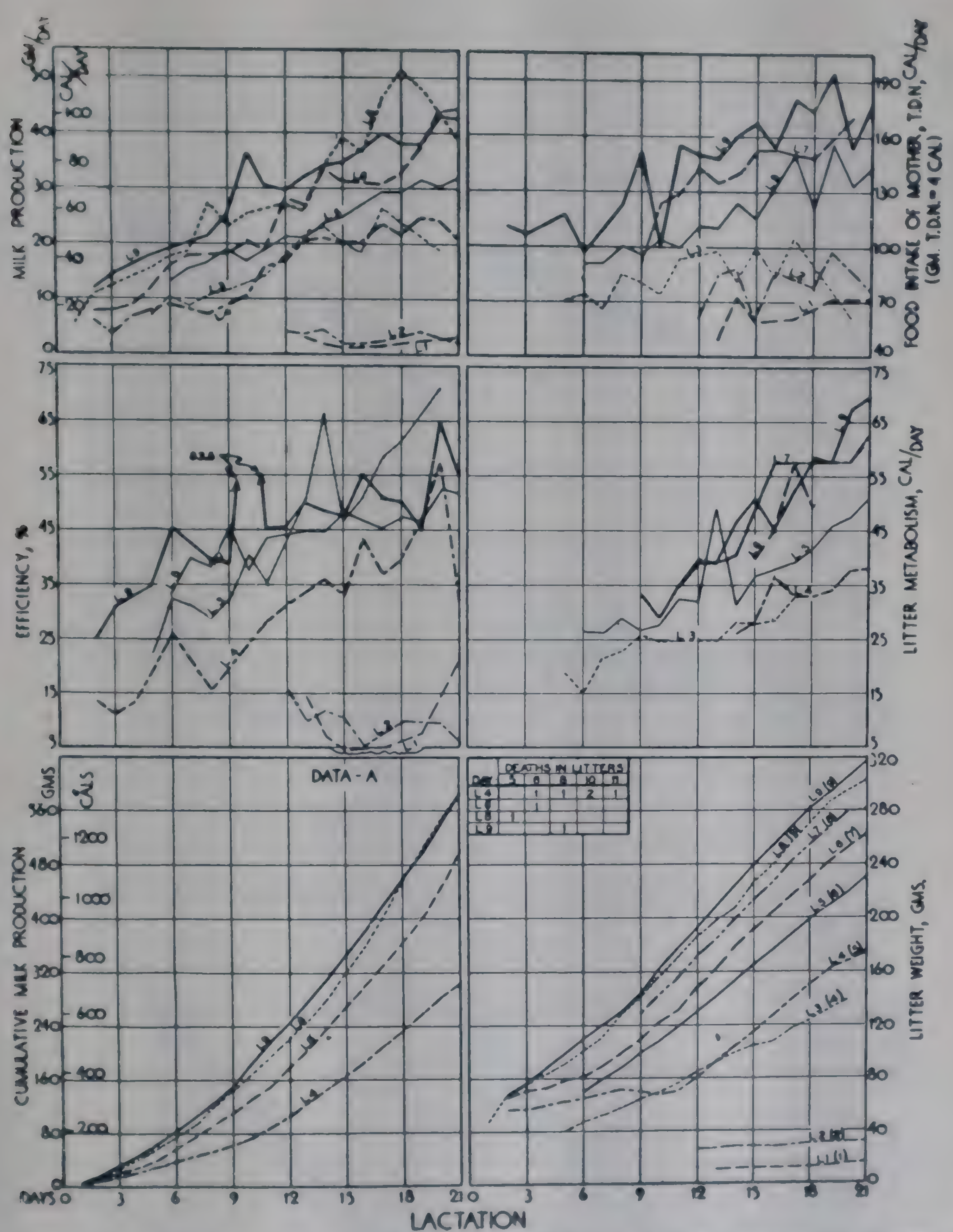

Fig. 21.12a. Milk production and energetic efficiency of milk production in rats in relation to stage of lactation, litter size, litter weight, food intake of mother rat, and litter metabolism. The energetic efficiency of milk production was obtained by two methods, method A (Fig. 21.12a), method B (Fig. 21.12b), and by both methods, A and B (Fig. 21.12c). Note that the rats produced 15 to 115 Cal. (av. 60 Cal.) milk per day, and 700–1400 Calories during the 21-day lactation period; that the mother rats consumed 70–220 Cal. TDN per day, depending on litter size (milk production). The numbers in parenthesis represent number of rats in litter. Fig. 21.12c compares the results obtained by methods A and B directly. Note that method A yields lower values than method B on animals A in the early stages of lactation, and higher values in the late stages. This discrepancy is due to: 1) increasing fuel value of the weight gains of the litter with increasing age, while in computing results it was assumed that the fuel value per gram gain is constant; 2) decreasing fuel value per gram milk with increasing milk production, while in computing results it was assumed that the fuel value per gram milk is constant.

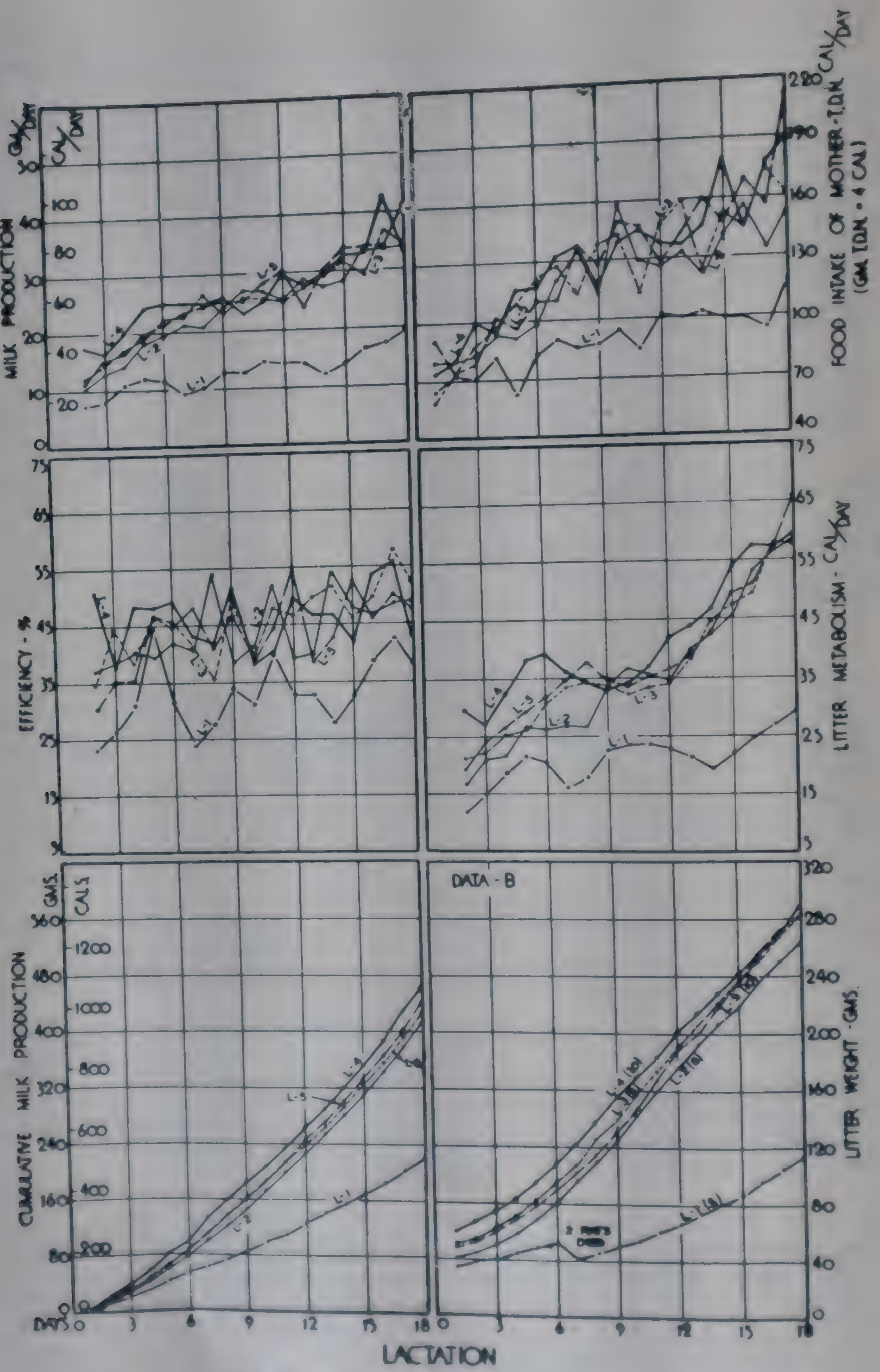

Fig. 21.12b. See legend for Fig. 21.12a.

$$\begin{array}{c}\text{Gross efficiency of}\\ \text{milk secretion in}\\ \text{the rat}\end{array} = \frac{\begin{array}{c}\text{Energy stored in the litter +}\\ \text{maintenance cost of litter}\end{array}}{\text{Calories } TDN \text{ consumed by mother}} \qquad \text{(B)}$$

The maintenance cost was estimated from the respiratory exchange (heat production); the stored energy, by multiplying the weight gains in grams by 1.5, assuming that 1 gm. body weight gain is equivalent to 1.5 Calories.

Fig. 21.12a to c present the results on milk production, and energetic efficiency of the rat as obtained by methods (A) and (B) above.

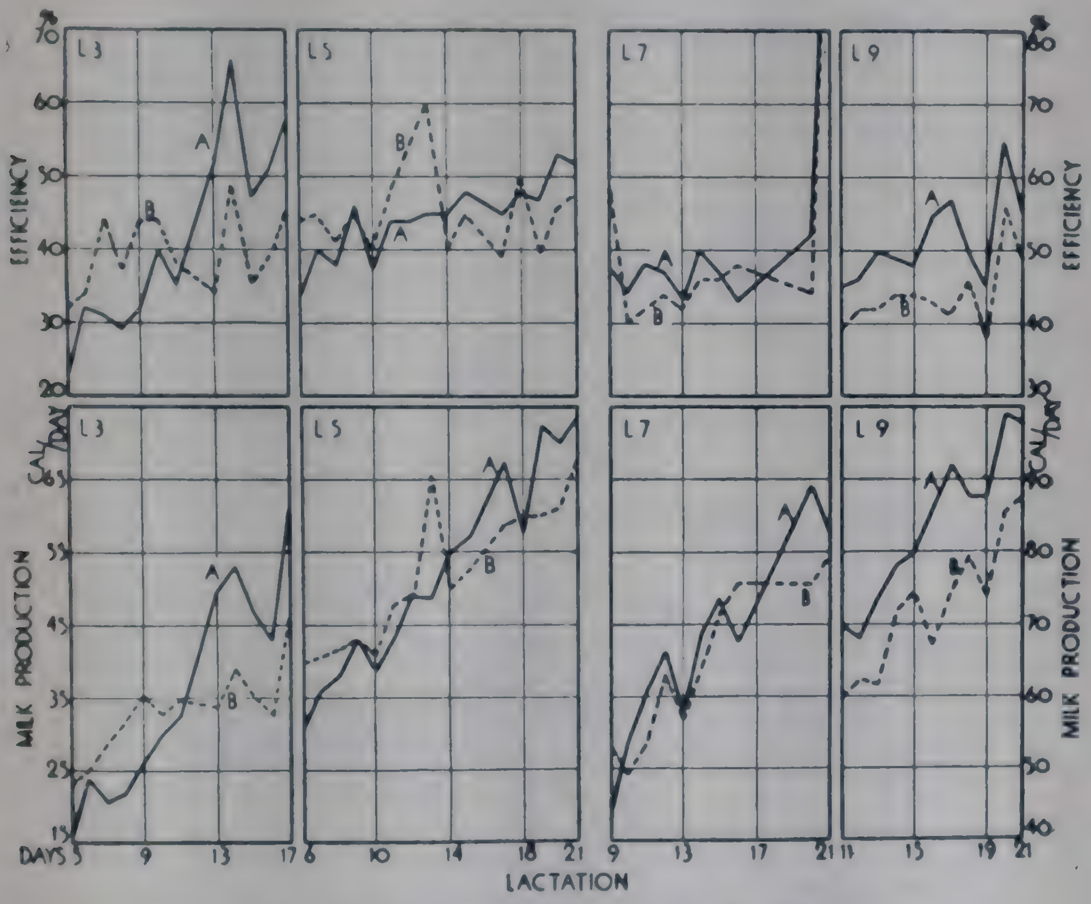

Fig. 21.12c. See legend for Fig. 21.12a.

The gross efficiency of milk production in the rat, in the flush of lactation, between the 10th and 18th, is seen from Fig. 21.12 to be between 44 and 48 per cent, which is of the same order as in the *champion* cows. The milk-production efficiency of the rat is higher than that of the *average-superior* experiment station cows, perhaps because the rats were on a relatively better (high-milk cereal) diet than the cattle (grain-hay); or perhaps because rats—raising large litters in a few days—are lactationally superior to cattle—raising 1 calf during a relatively long period. The important fact is that the gross energetic efficiency of milk production in the rat during the flush of lactation is of the same *order* as in cows or goats.

21.6.4: Influence of body size on gross efficiency of milk production. It is said that large animals are better milk producers than small ones because, as a rule, they produce more milk[155]. It is also said that small animals are better milk producers than large because (other conditions being equal) small animals produce more milk *per unit body weight* than large. Thus, as explained above, the average milk Calories produced per kg body weight are about 175 for rats and 25 for dairy cows.

However, the comparison of milk production in the preceding section shows that the *energetic efficiency* of milk production (the ratio of milk energy produced to food energy consumed, or "dairy merit") is virtually the same in rats, goats, humans, and cattle. We thus conclude that differences of opinion concerning the influence of body size on milk production are due to differences

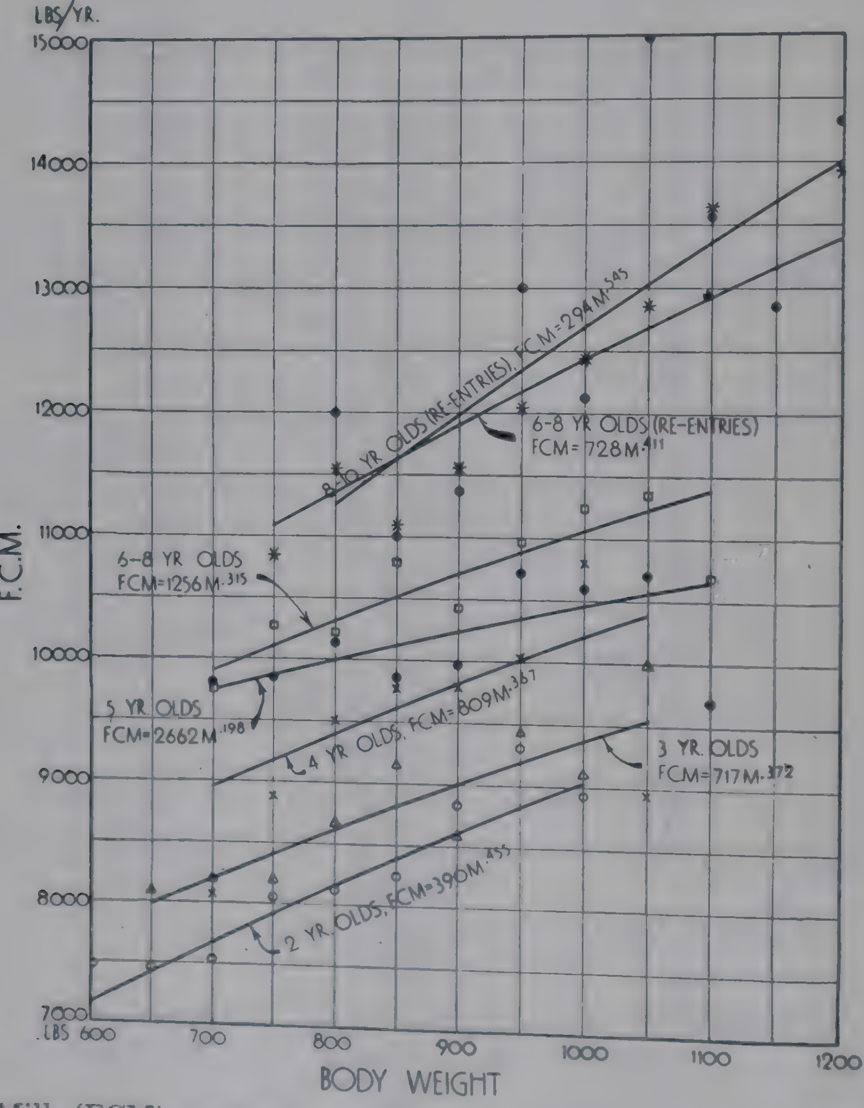

Fig. 21.13. Milk (FCM) production as function of body weight of 2-year old, 3-year old . . . Jersey cattle. Data compiled and averaged from the Jersey *Register of Merit* yearbooks 1918, 1920, and classified by ages as follows: 849 records, age 23–25 months (2 yrs.); 338 records, age 35 7 mos. (3 yrs.); 304 records, age 47–47 mos. (4 yrs.); 245 records ages 59–61 mos. (5 yrs.); 581 records 6–8 yrs.; 449 records 6–8 yrs., re-entries; 191 records 8–10 yrs., re-entries.

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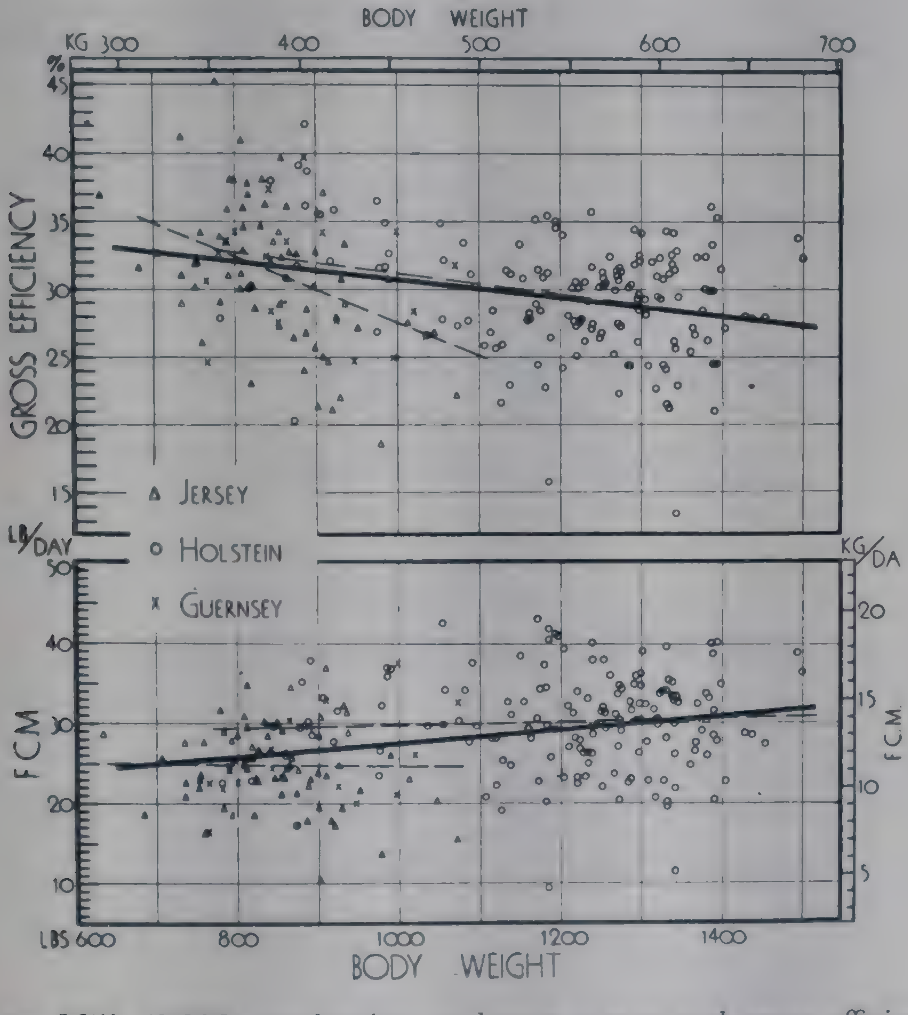
[155] Cf. McDowell, J. C., U. S. Dept. Agr. Cir. 114, 1930. According to dairy-cattle herd improvement association data, there is an increase in yearly yield of approximately 10 lb butterfat or 250 lbs FCM per 100 lbs increase in live weight. Under official test conditions, there is an increase of about 20 lbs butterfat or 500 lbs FCM for each 100-lb increase in body weight.

in the reference bases employed (Ch. 13). The fact is that when other conditions are equal, a large animal produces more milk *per animal* than a small animal; a small animal produces more milk *per unit weight* than a large animal; large and small animals produce the same amounts of milk energy *per unit food energy*. This problem of influence of body size on milk production, with special reference to practical (monetary) implications, is discussed in the following chapter (Sects. 22.2, 22.3, and Table 22.1).



Figs. 21.14a. Milk (FCM) production on lower curves and gross efficiency of milk production on upper curves. Fig. 14a represents the 243 experiment station cows listed in the table at the end of this chapter; the other curves are also plotted from the same table, as indicated. While FCM production usually rises with increasing body weight, efficiency usually declines. Further details are given in Univ. Missouri Res. Bulls., 222, 238, 239.

Small dairy cows are frequently more efficient energetically than large ones (Fig. 21.13 and 14). This is not due to body size *as such* but because the basis for selection has been the production *per cow*. To stay in the herd the small cow has had to produce nearly as much as the big one; but if the small cow produces as much as the big cow, she is more efficient because she has a smaller body and maintenance and therefore expends less of her feed for maintenance.

Figs. 21.13 and 21.14 also show how milk production tends to rise with body weight in cattle. **This problem is discussed in Chapters 13 and 22.**

It thus appears from the above analysis of lactation data of cattle, goats, rats, and humans that body size *as such* does not influence the energetic effi-

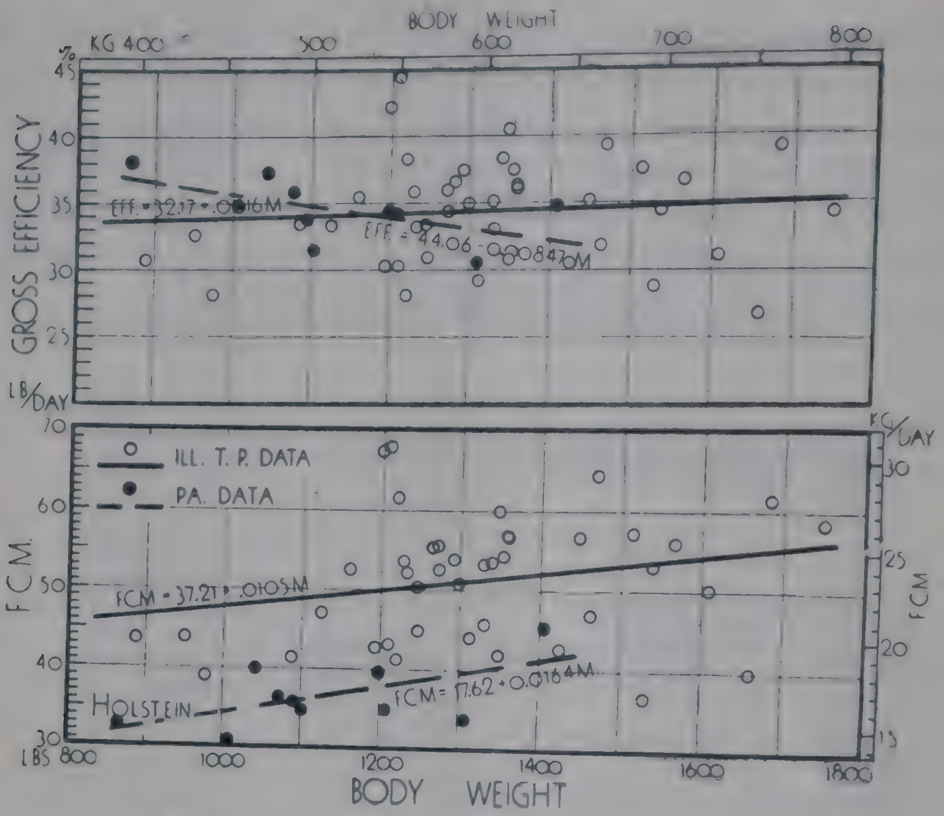


Fig. 21.14b. See legend for Fig. 21.14a.

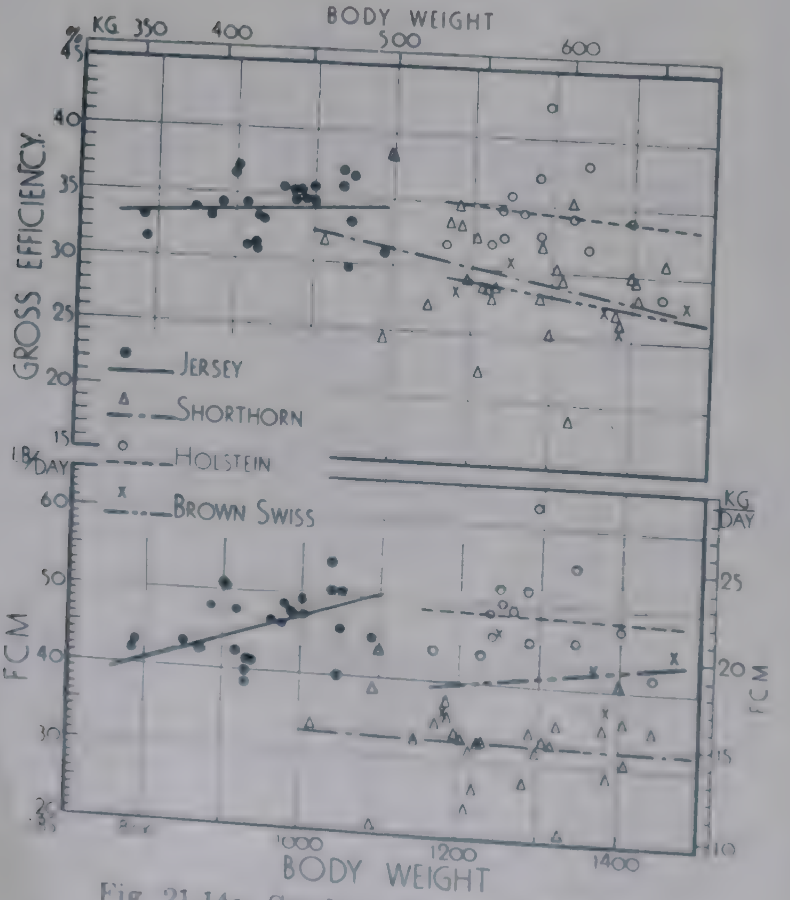


Fig. 21.14c. See legend for Fig. 21.14a.

ciency of milk production; other conditions being equal, small and large animals convert the same percentage of food energy into milk energy.

The gross efficiency of milk production of good dairy cattle with respect to TDN energy consumed[156] is of the order of 30 per cent. However, it appears from indirect evidence that at the biologic limit, that is, in the highest-producing champions, the gross efficiency may rise to 50 per cent. Following the psychologist's I.Q. (intelligence quotient) concept we may say that if the gross efficiency of milk production of the "average good" cow is 30 percent, and if a given champion cow's gross efficiency is 50 per cent, the L.Q. (lactation quotient) of the champion cow is 48/30 = 160. A cow having a L.Q. of 166 is a "lactational genius", just as a man having an I.Q. of 166 is an "intellectual genius".

21.6.5: Net efficiency of milk production. Having found that the average *gross* efficiency (including maintenance cost) of milk production of good dairy cattle is of the order of 30 per cent and of champion cows, at the biologic limit near 50 per cent, we next proceed to investigate the *net* energetic efficiency (excluding maintenance cost) of milk production. It is true that from the economic viewpoint the overall or gross efficiency is the more important; but we shall see that the net efficiency is also of considerable interest.

It was previously noted that the net efficiency of milk production with respect to TDN consumption is of the order of 60 per cent. The following discussion indicates how this value was obtained.

To evaluate the net efficiency, it is necessary to determine how much of the consumed *TDN* is used for (1) producing milk, (2) maintaining the animal, (3) gaining (or losing) body weight.

The partition of the feed for its various uses is evidently a problem of great difficulty. This cannot be done by a direct experimental approach. Accordingly, we devised an indirect statistical approach as follows[146].

Assume that the *TDN* is used for only the three purposes: producing milk, maintaining the cow, and gaining weight; and write this statement in the form of an equation:

$$TDN = B(FCM) + C(W^{0.73}) + D\Delta(W) \qquad (21.4)$$

in which TDN = total digestible nutrients consumed; FCM = 4 per cent milk produced; $W^{0.73}$ = live weight raised to the 0.73 power; ΔW = gain or loss in body weight. When other variables are held constant, B and D represent, respectively, units of TDN required to produce unit of 4 per cent milk, FCM, and to gain unit live weight, ΔW. The TDN cost of maintenance is C times body weight raised to the 0.73 power.

Then fit the equation to the data by the method of least squares, that is, by minimizing the squares of the residuals with respect to the three constants, B, C, D. This we did to the yearly lactation records of the 243 experiment station (Table 21.5) Holstein and Jersey (and a few Guernsey) cows 5 years of age or over (to eliminate age complications). The energies expended for converting milk precursors into milk and for the process of secretion are lumped with the FCM term. Solving in terms of pounds per day we obtain

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[156] The gross efficiency would be less if related to the gross instead of digestible energy consumed. Thus E. B. Forbes and A. Le Roy Voris, [*J. Nut.*, **5**, 395 (1932)] observed a gross efficiency of milk production of 18-23% when related to the gross energy of the ration.

$$TDN = 0.305FCM + 0.053\ W^{0.73} + 2.1\Delta W \tag{21.4a}$$

The meaning of the constants is as follows: if maintenance and weight-gain costs are held constant, 0.305 lb TDN is used per pound FCM produced; if milk yield and maintenance costs are held constant, 2.1 lbs TDN are used for 1 lb gain in live weight; if milk yield and weight gain costs are held constant, the TDN cost of maintenance is 0.053 time weight raised to the 0.73 power.

Note that equation (21.4) is based on the following unproved assumptions: TDN for FCM varies *linearly* with FCM production[157]; TDN for weight gain varies *linearly* with weight gain; TDN for maintenance is a power function, the power being 0.73, of body weight (so assumed because basal metabolism of mature animals of different species varies with the 0.73 power of body weight as explained in Ch. 13); TDN consumed is the algebraic sum of the above three terms—and no others.

The last assumption, that TDN consumption was not affected by factors other than FCM, W, and ΔW, may be tested by adding another constant, A, to take up the other unknown influencing factors, as indicated by the equation

$$TDN = A + B(FCM) + C(W^{0.73}) + D\Delta(W) \tag{21.5}$$

Solving, we obtained

$$TDN = 0.478 + 0.303\ (FCM) + 0.051\ W^{0.73} + 2.18\Delta W \tag{21.5a}$$

Inspection of eq. (21.5a) shows that the value of A, that is, 0.478 lb TDN, is small in comparison to the total TDN consumed by a lactating cow (av. for the 243 cows, 17.6 lbs TDN); moreover, the values of B, C, and D are inappreciably affected by omitting A (from 0.305 to 0.303 for B; from 0.053 to 0.051 for C; from 2.1 to 2.18 for D). Furthermore, the values of the statistical constants are very satisfactory for eq. (21.4).

From equation (21.4a) it is clear that if the overhead maintenance cost is not included, 0.305 lb TDN, or 553 Cal ($0.305 \times 1814 = 553$), are on the average used to produce 1 lb, or 340 Cal, FCM. The ratio of 340, the Cal in 1 lb FCM, to 553, the Cal in the TDN required to produce 1 lb FCM, that is, 0.61 or 61 per cent, is the *net* efficiency of milk production; it is the efficiency of converting TDN into milk, apart from the maintenance cost.

Gaines[158], employing a different approach, found that $B = 0.305$, exactly the same value as found by us. For maintenance, however, he found the second term of our equation (21.4a) to be not 0.05 $W^{.73}$, as we found, but 0.129 $W^{.60}$ "which two equations give the same results . . . when $W = 937$, and do not differ by more than 8 per cent at other values of W from 600 to 1800 lbs." "Furthermore, there is little choice between $n = 0.60$ and $n = 0.73$; while $n = 0.73$ is distinctly indicated in preference to $n = 1.00$. The lumped data, therefore, support the validity of Brody and Procter's working exponent 0.73 in preference to Haecker's exponent 1.00, or Morrison's exponent 0.87.

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[157] In the original report (Univ. Mo. Agr. Exp. Sta. Res. Bull. 238, pp. 47–9) an attempt was made to evaluate the exponent n in the equation

$$TDN'' = B(FCM)^n$$

in which TDN'' is total TDN consumed, less TDN used for maintenance ($CW^{.73}$) and for weight gain ($D\Delta W$). The numerical value of n ranged from 1.5 for low producing groups of cows to 0.34 for high producing groups of cows. The interested reader is referred to this bulletin, and more especially to Gaines, W. L., *J. Dairy Sci.*, **20**, 583 (1937).

[158] Gaines, W. L., *J. Dairy Sci.*, **20**, 583 (1937), and **21**, 645 (1938).

When we examine the similar data for various subgroups, great confusion develops." This confusion led Gaines to an examination of the maintenance feeding standards shown in Fig. 15.3, to suggest that "perhaps some factor not closely associated with live weight plays a prominent part" and to decide that for the present both, FCM production and maintenance TDN consumption, should be related to simple body weight, W, rather than to a fractional power, n, of body weight. He suggested using the Haecker milk-production feeding standard modified to $TDN = 0.3FCM + 0.008\,W$, in which FCM is 4 per cent milk and W live weight, all in pounds, as contrasted to the present author's feeding standard $TDN = 0.305FCM + 0.053\,W^{.73}$. There is obviously no appreciable difference between the two for average-sized cows (about 1000 lbs). The differences concern only extremely small and extremely large cows and only as they relate to maintenance, not to milk production.

The values in equation (21.4a) may be used for computing the net efficiency of milk production.

The net efficiency term may be isolated from the gross-efficiency equation,

$$\text{Gross efficiency} = \frac{340 \times FCM\ (\text{lbs})}{1814 \times TDN\ (\text{lbs})} \tag{21.3a}$$

by remembering that the denominator includes: (1) TDN expense of maintenance, represented in eq. (21.4a) by $0.053\,W^{0.73}$; and (2) weight gain, represented in eq. (21.4a) by $2.1\Delta W$. On substituting (1) and (2) from eq. (21.4a), we obtain:

$$\text{Gross efficiency} = \frac{340FCM}{1814\ (0.305FCM + 0.053W^{0.73} + 2.1\Delta W)}$$

$$= \frac{340FCM}{553FCM + 96.1W^{0.73} + 3700\Delta W}$$

Dividing the numerator and denominator by 553 (the TDN calories required to produce 1 lb FCM) presents net efficiency, 0.61, as a separate term in the gross efficiency equation

$$\text{Gross efficiency} = 0.61\,\frac{FCM}{FCM + 0.173W^{0.73} + 6.64\Delta W}$$

which is similar to Gaines' "coefficient of efficiency",[159]

$$\text{C. E.} = 52.6\,\frac{FCM}{FCM + 8.47W}$$

The net-efficiency equation

$$\begin{matrix}\text{Net efficiency}\\ \text{of milk production}\end{matrix} = \frac{\text{milk calories produced}}{TDN\ \text{calories consumed less maintenance}} \tag{21.2}$$

may also be written by substituting the values of eq. (21.4a) into it, as follows:

$$\text{Net efficiency} = \frac{340FCM}{1814\ [TDN - (0.053W^{0.73} + 2.1\Delta W)]}$$

The 61 per cent net-efficiency level is, of course, only a statistical average, for the given conditions, computed by the given method, and not applicable to an individual cow.

The detailed method of solving the partition equation (21.4) is shown in the appendix to this chapter. The numerical data for the individual cows are also listed in the appendix (Table 21.7).

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[159] Gaines, W. L., *Science*, **67**, 353 (1928).

Summarizing, this section presents a statistical method for partitioning the *TDN* consumed between maintenance, milk production and body weight gain, and computing therefrom net efficiency of milk production with respect to *TDN* consumption. It must be emphasized that the numerical value of the net efficiency would be much less if it were computed with respect to the gross energy of the feed; and much higher if it were computed with respect to metabolizable energy, and still higher—perhaps 90 or 95 per cent as found by Graham (previously discussed)—if it were computed with respect to net energy or to the milk-precursor energy entering the mammary gland.

It is evident that the *gross* energetic efficiency of milk secretion, which carries the burden of the maintenance cost of the cow, can never be as great as the *net* efficiency, which is not thus burdened with maintenance taxes. As production increases, the maintenance tax per unit milk produced becomes less and less; therefore, the gross efficiency approaches nearer and nearer to the net efficiency level, but at *decreasing increments*, in accordance with the law of diminishing returns. The relation between gross efficiency and milk production (FCM) level is shown in Fig. 1.2 (Ch. 1). Since the net efficiency of milk production is of the order of 60 per cent, the gross efficiency can never reach 60 per cent, but it may approach 50 per cent. This checks with the estimated gross efficiency for the 700-lb Jersey champion cow Stonehurst Patrician's Lily, previously cited.

21.7: Summary. This chapter discusses the following problems.

(1) The dairy industry and its place in the national, especially agricultural, economy. Dairy husbandry is the largest branch of agriculture from the viewpoint of return to the farmer and number of persons employed.

(2) The unique composition of milk, most conspicuously its lactose, casein, short-chain fatty acids, minerals, especially calcium and vitamins. The composition of milk is loosely related to the percentage growth rate or maturation rate of the body.

(3) The unique composition of milk is associated with its unique nutritional properties. Milk was evolved especially for the nutrition of young mammals and has a matchless combination of protein of high biologic value, of calcium, phosphorus and vitamins. It is poor, however, in iron, copper, manganese, and apparently magnesium, Milk happens to supplement almost perfectly whole-cereal diets for adult humans. Almost $\frac{1}{5}$ of the dietary energy consumed in this country in "adequate" and "liberal" diets comes from milk. The skimmilk-butter-margarine problem is discussed in some detail.

(4) From the viewpoint of relative energetic economy of meat, egg, and milk production, the gross efficiency of *early* growth and of average milk production is of the same order. As, however, the animal increases in size, its efficiency for meat production decreases rapidly because of the mounting maintenance cost in comparison to the growth increments. Moreover, much of the animal body is inedible, whereas all of milk is edible. Furthermore, with the exception of some visceral organs, as liver and kidney, milk has unique supplementary properties not found in meat. Finally, the possibility of in-

creasing the energetic efficiency of milk production (by improved breeding methods) is greater than for meat production. In general, the gross *energetic* efficiency of milk production tends to be about twice that of egg production and about five-fold that of meat production (Ch. 3).

(5) Physico-chemical considerations of milk production indicate complex interdependence between osmotic and enzymatic factors and between the protein, fat, lactose, and water constituents. Milk sugar is produced not only from blood sugar, but also from blood lactic acid and from amino acids. Milk fat is derived mostly from blood fat, and milk protein from blood protein and amino acids.

(6) It is shown that there is a considerable heat increment of lactation. It is not possible to measure the *basal* metabolism of lactation because the post-absorptive condition requisite for basal metabolism depresses the milk flow so that lactation is no longer normal.

(7) It is shown that good experiment-station dairy cattle (for example, 1100-lb cows producing about 35 lbs FCM per day and consuming 21 lb TDN per day) produce milk at a gross energetic efficiency near 33 per cent with respect to TDN consumed, that is, about one-third of the TDN fed a good cow is recovered in the milk. By proper breeding, the gross efficiency may be increased to a maximum near 50 per cent. The *net* efficiency of milk production (not counting the maintenance cost) with respect to TDN consumption is shown to be of the order of 60 per cent.

(8) The gross energetic efficiency of milk production is apparently independent of live weight as such. It is true that the ratio of milk-energy yield to body weight is greater in small animals, such as 120-lb goats, than in large animals such as 1200-lb cows; but the ratio maintenance-energy cost to body weight is likewise greater for the 120-lb goat than for the 1200-lb cow, with the net result that the extra maintenance cost counterbalances the extra milk yield and the gross efficiency is unaffected by body size.

(9) The appendix indicates the method for fitting the "partition equation," partitioning the food consumption between maintenance, milk production, and body gain; and presents numerical data on milk production, feed consumption, body weight, and related items.

Appendix: Estimating the amounts of consumed TDN used for FCM production, maintenance, and weignt gain (solution of eq. (21.4a)). The partition of the consumed *TDN* between its uses for each, *FCM*, maintenance ($W^{.73}$), and weight gain (ΔW), may be carried out graphically, or algebraically by the method of least squares.

The graphic method consists in plotting *TDN* successively against each of the independent variables, namely *FCM*, $W^{.73}$, and ΔW; correcting observed *TDN* values for the influence of one variable by approximating *TDN* cost per unit of that variable; subtracting computed *TDN* required for the one variable from the observed *TDN* for each datum; correlating corrected *TDN* with another variable and determining a second correction. These first approximations of the parameters are improved by successively repeating this process of approximation until the sum of the squares of the differences between observed and computed *TDN* is minimum. .

The least-squares method eliminates the laborious successive approximations. The solution of the partition equation

$$TDN = B(FCM) + CW^{.73} + D\Delta W \tag{21.4}$$

by the least-squares method involves substituting in three "normal equations" simultaneously, and weighting the trends of TDN with FCM, W, and ΔW so as to give at once a minimum value for the sum of the squares of the differences.

An obvious objection to equation (21.4) is that it was formulated on the assumption that the milk secretion, maintenance, and weight-gain factors are independent. This is by no means certain. Moreover, since the coefficients in the equation are computed by the method of least squares, it is clear that if the value of one coefficient is too high due to some experimental or biological situation, the values of the other coefficients will be influenced thereby. Each of the terms represented in equation (21.4) has its separate set of experimental errors and biological variations. When combined into one interrelated system, each of these terms influences the value of every other term. There consequently results a very complex system of interinfluencing relationship.

A large population compensates and smoothes out individual experimental errors and biological variations so that dependable average values for the equation constants B, C, and D result. But if a small population is combined with large errors and variations, the equation constants are no longer dependable, and are often absurd, as illustrated by the following numerical examples.

The aforementioned three "normal equations" for equation (21.4) are:

$$\begin{aligned}
\Sigma(TDN)(FCM) &= B\Sigma(FCM)^2 + C\Sigma(FCM)(W^{0.73}) + D\Sigma(FCM)(\Delta W)\\
\Sigma(TDN)(W^{0.73}) &= B\Sigma(FCM)(W^{0.73}) + C\Sigma(W^{0.73})^2 + D\Sigma(W^{0.73})(\Delta W)\\
\Sigma(TDN)(\Delta W) &= B\Sigma(FCM)(\Delta W) + C\Sigma(W^{0.73})(\Delta W) + D\Sigma(\Delta W)^2
\end{aligned}$$

Taking, by way of illustration, the data for the 15 World's Fair Holsteins listed in Table 21.6, we obtain the following summations:

$\Sigma(TDN)\ (FCM) = 19525.1508$
$\Sigma(TDN)\ (W^{0.73}) = 74486.866$
$\Sigma(TDN)\ (\Delta\ W) = 327.95458$
$\Sigma(FCM)^2 = 36129.7151$
$\Sigma(FCM)\ (W^{0.73}) = 136482.688$
$\Sigma(FCM)\ (\Delta\ W) = 593.90690$
$\Sigma(W^{0.73})^2 = 522017.86$
$\Sigma(W^{0.73}\ (\Delta\ W) = 2303.8917$
$\Sigma(\Delta\ W)^2 = 11.251476$
$\Sigma(TDN)^2 = 10642.4553$

Substituting in the "normal equations" we have:

$$\begin{aligned}
1952.1508 &= B\ 36129.7151 + C\ 136482.688 + D\ 593.90690\\
74486.866 &= B\ 136482.688 + C\ 522017.86 + D\ 2303.8917\\
327.95458 &= B\ 593.90690 + C\ 2303.8917 + D\ 11.251476
\end{aligned}$$

Solving these equations we obtain $B = 0.11642$, $C = 0.11146$, and $D = 0.18040$, *i.e.*, $TDN = 0.116\ FCM + 0.11W^{0.73} + 0.180\Delta W$. Illustrating the solution by Doolittle's method[160] we have:

Line	Reciprocals	*B*	*C*	*D*	—	Sum
I		36129.7151	136482.688	593.90690	−19525.1508	153681.15920
II			522017.86	2303.8917	−74486.866	586317.5737
III				11.251476	−327.95458	2581.095496
1		36129.7151	136482.688	593.90690	−19525.1508	153581.15920
2	−.0000276780483	−1.00000000	−3.77757443	−.016438184	.5404018067	−4.253594542
3			522017.86	2303.8917	−74486.866	586317.5737
4			−515573.51	−2243.5275	73757.710	−580542.0166
5			444.35	60.3642	−729.156	5775.5571
6	−0.000155174587		−1.0000000	−.009366996	.113146554	−896220265
7				11.251476	−327.95458	2581.095496
8				−9.762751	320.95802	−2526.239169
9				−.565431	6.83000	−54.099620
10				.923294	−.16656	.756707
11	−1.08307862			−1.0000000	.180397576	−.819573

$D = .180397576$
$C = .111456771$
$B = .116416411$

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[160] See Ezekiel, M., "Method of correlation analysis," New York, 1930, Ch. 12. See also, Mills, F. C., "Statistical methods applied to economics and business," New York, 1924, p. 577.

The standard error of estimate for equation (21.4a) is

$$S_r^2 = \frac{(TDN)^2 - B(TDN)(FCM) - C\Sigma(TDN)(W^{0.73}) - D\Sigma(TDN)(\Delta W)}{N}$$

where N is the "degree of freedom." The "degrees of freedom" is the number of data points less the number of arbitrary constants in the equation fitted; thus $N = 15 - 3 = 12$.

Substituting:

$$S_r^2 = \frac{10642.4553 - (.11642 \times 19525.1508) - (.11146 \times 74486.866) - (.18040 \times 327.95458)}{12}$$

$$S_r^2 = \frac{10642.4553 - 2273.1181 - 8302.3061 - 59.1630}{12} = \frac{7.8681}{12}$$

$$S_r^2 = 0.655675$$

$$S_r = 0.810$$

The standard error of estimate, $S_r = 0.81$, means that two-thirds of the time the *TDN* computed from this equation will agree with the observed *TDN* consumption within ± 0.81 lb.

This small value of S_r leads one to think that the numerical values of B, C, and D are significant and reliable. As a matter of fact these values are so far out of line that they must be considered meaningless. Thus the maintenance of a 1000-lb cow is, according to this equation, $0.1115 \times 1000^{.73} = 17$ lbs, which is over twice the Morrison allowance of 7.9 lbs, and therefore absurd. The net efficiency is, according to this equation, $\frac{340 \times 100}{.1164 \times 1814} = 164$ per cent, which is of course impossible. In other words, of the available *TDN*, far too much is apportioned by this equation to maintenance, and far too little for milk production (and for weight gain).

Does this mean that equation (21.4) is wrong? Not necessarily. It means that the number of animals in the population is too small in comparison to the variability. The data points are too irregular and too few to give the equation a lead, so to speak, to the real situation. The three sets of guide posts involved in showing the road (*TDN* trends for *FCM* production, maintenance, weight gain) are so few, and distributed so erratically, that they are blurred and therefore useless as guides for reaching the desired goal.

It is not the fewness of the data that is alone responsible for the erratic results, as the *combination* of fewness, limited range, and erratic distribution of data. The erratic distribution of the data is probably due to their experimental errors. Better (even if fewer) data give better results. Thus equation (21.4) fitted to only 10 of the Pennsylvania Animal Nutrition Institute (Forbes) data gave entirely satisfactory results. In this case the value of C for equation (21.4) was found to be 0.053, so that the maintenance for a 1000-lb cow is 8.2 lbs (which is the average of the value found for the 243 Experiment Station cows (Fig. 21.14a); the value of B was found to be 0.292, indicating net efficiency of 64 per cent (in comparison to 61 per cent found for the 243 experiment Station cows). This brings us back to the statement that reliability of the equation parameters is conditioned on accuracy of the data. To summarize, equation 21.4 gives dependable average values separately, for *FCM* production, maintenance, weight-gain but only provided that the population is reasonably large and the data are reliable.

TABLE 21.1. COMPARISON OF THE NATIONAL RESEARCH COUNCIL (1943) NUTRITIONAL-NEED STANDARD FOR A 70-KG MODERATELY ACTIVE MAN WITH THE NUTRIENTS SUPPLIED BY ONE QUART OF RAW MILK.

Nutrients	Average daily requirement for a 70-Kg, (154-lb) adult	Amount in one quart milk	Approximate portion of the daily requirement supplied by one quart raw milk
Protein (gm)	70	34	$\frac{1}{2}$
Calories	3000	675	$\frac{1}{4}$
Calcium (gm)	0.8	1.16	$1\frac{1}{2}$
Phosphorus (gm)	1.3	0.91	$\frac{2}{3}$
Iron (mg)	12	1.94	$\frac{1}{7}$
Vitamin A[12] (I.U.)	5000	1900	$\frac{2}{5}$
Vitamin D[12] (I.U.)	400	25	$\frac{1}{16}$
Ascorbic acid[13] (mg)	75	19.4	$\frac{1}{4}$
Thiamine (mg)	1.8	0.28	$\frac{1}{6}$
Nicotinic acid (mg)	18	1.1	$\frac{1}{16}$
Riboflavin (mg)	2.7	1.7	$\frac{2}{3}$

The Calories in milk are divided equally between fat and non-fat fractions:

Constituent	Grams/quart	Calories/quart
Fat	37	333
Lactose	49	196 } 332
Protein	34	136 }

TABLE 21.2 FATTY ACID COMPOSITION OF FAT IN MILK AND BEEF PLASMA.

Saturated acids	Carbons	Percentage by weight in: milk	beef plasma
Butyric	4	3.7	
Caproic	6	2.0	
Caprylic	8	1.0	
Capric	10	2.6	
Lauric	12	1.7	
Myristic	14	8.3	0.4
Palmitic	16	25.4	24.5
Stearic	18	10.7	12.3
Arachidic	20	0.4	0.8
Unsaturated acids			
Deconoic	10	0.2	
Tetradecenoic	14	1.2	
Hexadecenoic	16	5.0	2.5 (Palmitoleic)
Oleic	18	32.4	17.4
Octadecenoic	18	4.0	
C 20 to 22 unsat.	20–22	0.4	1.3 (Arachidenic)
Linoleic			36.5
Linolenic			4.2

TABLE 21.3 COMPOSITION OF MILK OF DIFFERENT SPECIES AND GROWTH RATE. (After Abderhalden, modified, enlarged with averaged data from various sources and percentage-distribution sections added.)

Species	Growth rate (days for doubling body weight)	Constituents as percentages of whole milk						Constituents as percentages of milk solids				Caloric values of constituents as percentages of caloric values of milk			Fuel value Cal/gm
		Fat	Protein	Lactose	Ash	Water	Total solids	Fat	Protein	Lactose	Ash	Fat	Protein	Lactose	
Cow	70 (47)	4.4	3.8	4.9	0.7	86.2	13.8	32	27	36	5.1	53	20	26	.75*
Goat	22	4.1	3.7	4.2	0.8	87.1	12.9	32	29	33	6.2	54	22	24	.75*
Man	180	3.8	1.6	7.0	0.2	87.4	12.6	30	13	56	1.6	50	9	41	.68
Horse	60	1.6	2.7	6.1	0.5	89.0	11.0	15	25	56	4.6	29	22	49	
Ass		1.5	2.1	6.4	0.3	89.7	10.3	15	20	62	2.9	28	18	54	
Camel		5.4	3.0	3.3	0.7	87.6	12.4	44	24	27	5.6	66	16	18	
Sheep	35 (15)	6.2	5.4	4.3	0.9	82.9	17.1	37	32	26	5.4	59	23	18	.98
Reindeer		22.5	10.3	2.5	1.4	63.3	36.7	61	28	7	3.8	80	16	4	2.4
Pig	14	7	6	4	0.9	83	17	39	34	22	5.0	64	24	12	
Dog	9	8.5	7.5	3.7	1.2	79	21	41	36	18	5.7	63	25	12	
Cat		5	7	5	0.6	82	18	28	40	28	3.4	48	30	22	
Rabbit	6	16	14	2	2.2	65	35	47	41	6	6.4	69	27	4	
Rat	6	15	12	3	2.0	70	30	47	38	9	6.2	69	25	6	
Guinea pig	7	7	5	2		85	15	50	36	13		69	22	9	
Elephant		15	4.9	3.4	0.8	73	27	62	20	14	3.3	80	12	8	
Whale		44 (22)	7 (12)	1.8	0.5	49	51	83	13	3	0.9	92	6	2	
Porpoise		49	11	1.3	0.6	38	62	79	18	2	1.0	90	9	1	
Dolphin		15	10	6		70	30	48	32	19		68	20	12	
Monkey		3.9	2.1	6	0.3	87.7	12.3	32	17	49	2.4	76	18	5	
Water buffalo		12	6	4	0.9	77.1	22.9	52	26	18	3.9	73	16	11	
Australian anteater		20	11	3	0.8	63	37	57	32	9	2.3	76	19	5	
Pigeon crop "milk"	2	8	13	0	1.5	77	23	36	58	0	6.7	42	58	0	

* The combustion value of goat's milk containing 4% fat is the same as for cow's milk containing 4% fat, namely, about 340 Cal/lb, or 0.75 Cal/gm.

TABLE 21.4. TIME CHANGES IN COMPOSITION OF COLOSTRUM MILK AFTER THE FIRST PARTURITION, AVERAGE OF TWO COWS.[79]

Time after calving	% of first milking										
	Total solids	Protein	Fat	Lactose	Ash	Ca	Mg	K	Na	P	Cl
(hrs)											
0	100	100	100	100	100	100	100	100	100	100	100
6	91	72	122	103	84	76	74	107	72	70	98
12	68	41	112	107	72	64	47	104	80	62	92
24	52	29	70	117	66	60	36	114	75	63	91
36–40	52	28	60	119	70	64	36	128	66	62	81
44–48	48	27	54	118	69	62	38	118	70	66	82
60–6	52	26	69	114	66	65	40	126	83	60	83
68–72	52	26	68	110	67	62	38	120	70	59	83
10–11 days	50	22	60	138	60	54	31	117	54	22	56

Time after calving	Each as percentage of all minerals						Each as percentage of total solids			
	Ca	Mg	K	Na	P	Cl	Ash	Protein	Fat	Lactose
(hrs)										
0	28	4	16	10	26	15	5	54	26	14
6	26	3	22	8	22	18	4	44	35	17
12	24	2	22	10	23	18	6	32	39	23
24	23	2	25	10	22	18	6	39	34	31
36–40	24	2	28	8	23	16	6	29	29	35
44–48	24	2	26	9	22	16	6	30	28	35
60–64	24	2	26	10	20	17	6	28	34	32
68–72	24	2	26	9	22	16	6	28	34	32
10–11 days	26	2	32	8	24	13	6	23	31	40

TABLE 21.5. DATA ON THE UNITED STATES DAIRY INDUSTRY.

Year	Dairy cattle, million head			Annual milk production billion lbs.	Annual per capita consumption of dairy products, lbs						Cash farm income from dairy products million $/yr.
	Cows	Calves birth to 1 yr.	Calves 1 to 2 yrs.		All dairy products equivalent to whole milk	Fluid fresh milk	Butter	Cheese (except pot, bakers, and cottage)	Ice Cream	Evaporated whole milk	
1930	23.0	5.2	4.9	103	818	353	17.3	4.6	10	11.3	
1936	25.2	5.5	5.0	105	797	338	16.5	5.4	10	14.1	1387
1940	25.0	6.0	5.5	112	825	347	17.0	6.0	12	17.5	1517
1941	25.5	6.2	5.7	118	814	347	16.4	6.0	15	18.5	1897

TABLE 21.6 SUMMARY OF THE DATA IN TABLE 21.7 DISCUSSED IN SECTION 21.6.

Data	Factual							Speculative (i. e., computed on the basis of debatable assumptions.)			
								Constants of Equation TDN = B(FCM) + $CM^{0.73}$ + DΔM			
	No. of Cows	Av. Live Wt., Lbs.	Av. Daily Live Wt. Gains, Lbs./Day	Av. Daily FCM Production, Lbs./Day	Av. Daily TDN consumption, Lbs./Day	Av. Observed Gross Effic., %	Computed Net Effic. (from equation), %	B	C	D	Sr
Experiment Sta. (Res. Bull. 222)	243	1087	0.117	28.26	17.64	30.1	62.2	0.305	0.053	2.13	1.02
La.-Purchase Exposition:											
All breeds	73	1161	0.773	40.97	23.90	31.8	51.5	0.367	0.046	1.19	1.44
Brown Swiss	5	1208	0.675	41.49	27.78	28.0	42.8*	0.274	0.087	−0.319	
Holstein	15	1290	0.823	48.81	26.63	34.3	53.6*	0.116	0.111	0.180	
Jersey	25	948	0.599	45.59	25.09	33.6	48.7*	0.217	0.098	0.772	
Shorthorns	28	1252	0.920	32.56	20.69	29.6	54.3*	0.205	0.066	2.08	
Class A	45	1104	0.682	46.21	25.90	33.2	49.7*	0.263	0.083	−0.276	
Class B	65	1158	0.736	41.93	24.16	32.3	53.2*	0.373	0.047	0.510	
Class C	34	1280	0.859	35.69	22.60	29.6	51.9*	0.347	0.050	1.15	
Ill. Testing Plant Holsteins	42	1322	0.058	51.15	27.83	34.3	82.4	0.229	0.084	0.338	1.84
Forbes' Pa. Holsteins	10	1131	0.215	36.20	19.75	34.4	64.5	0.292	0.053	1.52	0.76
All of above	368	1130	0.243	33.64	19.96	31.0	53.6	0.350	0.046	1.88	1.43

Data	Milk (FCM) Production and Ratios									
	No. of Cows	Live Weight, Pounds	Absolute FCM Production/day		Ratios of FCM Calories produced to:				Observed Absolute TDN Consumption	
			Pounds	Calories	Computed Basal Metabolism, Calories	Observed Total Consumed TDN	Computed TDN Cals. for FCM Prod. Only	Computed Maintenance, Calories	Pounds	Calories
Experiment Station	243	1087	28.26	9608	1.48	0.30	0.61	0.61	17.64	32000
Exposition										
All Breeds	73	1161	40.97	13930	2.05	0.32	0.52	0.97	23.90	43355
Brown Swiss	5	1208	41.49	14107	1.87	0.28	0.43	0.88	27.78	50393
Holsteins	15	1290	48.81	16595	2.25	0.34	0.54	1.07	26.63	48307
Jerseys	25	948	45.59	15501	2.64	0.34	0.49	1.24	25.09	45513
Shorthorns	28	1252	32.56	11070	1.54	0.29	0.54	0.92	20.69	37532
Class A	45	1104	46.21	15711	2.40	0.33	0.50	1.13	25.90	46983
Class B	65	1158	41.93	14256	2.10	0.32	0.53	0.99	24.16	43826
Class C	34	1280	35.69	12135	1.66	0.30	0.52	0.78	22.60	41000
Illinois Testing Plant Holsteins	42	1322	51.15	17391	2.32	0.34	0.82	0.60	27.83	50483
Forbes' Pa. Holsteins	10	1131	36.20	12308	1.84	0.35	0.64	0.75	19.75	35736
Ave. of all groups	368	1130	33.64	11438	1.71	0.32	0.54	0.80	19.96	36207
Column number		C1	C2	C3	C4	C5	C6	C7	C8	C9

Footnotes: Column 2, observed; C 3 = C 2 × (340); C 4 = $\frac{C\,3}{C\,19}$; C 5 = $\frac{C\,3}{C\,19}$; 6 = $\frac{3}{14}$; 7 = $\frac{3}{15}$; 8 =, observed; 9 = 8 × (1814); 10 = $\frac{9}{19}$; 11 = $\frac{9}{16}$; 12 = $\frac{9}{3}$; 13 = 22 × 2; 14 = 13 × (1814). 15 = 23 × $M^{0.73}$ values of weight M, given in Col. 1; 16 = 15 × (1814); 17 = $\frac{13}{8}$; 18 = $\frac{15}{8}$; 19 = computed from, Basal metabolism (Cal) = $39.5M^{0.73}$ where M is live weight in pounds given in Col. 1; 20 = $\frac{16}{19}$; 21 = $\frac{14}{19}$.

TABLE 21.6. *Continued*

Data	Feed (TDN) Consumption, and Ratios									Computed Basal Met. and Ratios			Equation Constants	
	Ratio of TDN Calories Consumed to			Computed Daily TDN Consumption for				Computed Percentage Distribution of Consumed TDN Between		Computed Basal Metabolism, Cals./day	Ratio to Computed Basal Met. of Computed TDN, Cals.			
	Computed Basal Met., Calories	Computed Maintenance, Calories	Observed FCM, Calories	Milk Production		Maintenance								
				Pounds	Calories	Pounds	Calories	Milk Prod.	& Main.		Main.	Milk	B	C
Experiment Station	4.9	2.0	3.3	8.6	15637	8.7	15836	48.9	49.5	6475	2.4	2.4	0.305	0.053
Exposition														
All Breeds	6.4	3.0	3.1	15.0	27264	7.9	14403	62.9	33.2	6806	2.1	4.0	0.367	0.046
Brown Swiss	6.7	3.2	3.6	15.2	27627	8.8	15927	54.8	31.6	7527	2.1	3.7		
Holsteins	6.6	3.1	2.9	17.9	32489	8.6	15582	67.3	32.3	7363	2.1	4.4		
Jerseys	7.7	3.7	2.9	16.7	30348	6.9	12444	66.7	27.3	5881	2.1	5.2		
Shorthorns	5.2	2.5	3.4	12.0	21677	8.4	15256	57.8	40.7	7204	2.1	3.0		
Class A	7.2	3.4	3.0	17.0	30765	7.7	13877	65.5	29.5	6558	2.1	4.7		
Class B	6.5	3.0	3.1	15.4	27917	7.9	14385	63.7	32.8	6792	2.1	4.1		
Class C	5.6	2.7	3.4	13.1	23763	8.5	15492	58.0	37.8	7321	2.1	3.2		
Illinois Testing Plant Holsteins	6.8	1.8	3.0	11.7	21242	15.9	28861	42.1	57.2	7484	3.9	2.8	0.229	0.084
Forbes' Pa. Holsteins	5.3	2.2	2.9	10.6	19228	9.0	16326	53.7	45.6	6691	2.4	2.9	0.292	0.053
Ave. of all groups	5.4	2.5	3.2	11.8	21405	7.9	14331	59.1	39.6	6687	2.1	3.2	0.350	0.047
Column number	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23

TABLE 21.7. INDIVIDUAL MILK, FEED, AND BODY WEIGHT RECORDS OF COWS DISCUSSED IN THIS CHAPTER AND THE FOLLOWING CHAPTER.[161]

Average Live wt., lbs.	Feed TDN, lbs./day	Milk FCM, lbs./day	Live wt. gain, lbs./day	Gross Energetic Effic.		Profit per year, dollars*	
				Not corrected for wt. gain	Corrected for wt. gain	per cow	per 1000 lbs. FCM
"Louisiana Purchase World's Fair" Data							
Brown Swiss, 5							
1181	24.0	36.1	.550	28.3	29.0	132	10.1
1248	28.3	46.5	.617	30.8	31.6	184	10.8
1367	29.2	42.6	.417	27.4	27.8	151	9.7
1384	27.2	37.3	1.225	25.7	27.1	124	9.1
1467	30.2	44.9	.567	27.8	28.5	162	9.9
Holsteins, 15							
1167	25.8	43.7	.967	31.7	33.3	178	11.2
1225	25.5	43.5	.700	32.0	33.1	178	11.2
1236	26.5	48.8	1.392	34.5	36.8	211	11.8
1239	26.5	45.8	.750	32.4	33.5	189	11.3
1247	27.5	52.4	.567	35.7	36.6	232	12.4
1252	26.6	50.1	.842	35.3	36.7	220	12.0
1264	27.0	49.5	.725	34.3	35.4	213	11.8
1283	26.2	51.6	.717	37.1	38.3	235	12.4
1286	26.0	45.5	.975	32.8	34.3	190	11.4
1292	27.6	62.4	.450	42.5	43.3	305	13.4
1327	26.8	48.6	.967	34.1	35.6	208	11.8
1343	27.1	55.1	.767	38.1	39.4	254	12.6
1344	27.0	45.7	.308	31.8	32.2	186	11.2
1398	26.2	47.6	.992	34.0	35.6	204	11.7
1438	27.1	41.5	1.225	28.7	30.4	155	10.2

Average Live wt., lbs.	Feed TDN, lbs./day	Milk FCM, lbs./day	Live wt. gain, lbs./day	Gross Energetic Effic.		Profit per year, dollars*	
				Not corrected for wt. gain	Corrected for wt. gain	per cow	per 1000 lbs. FCM
Jerseys, 25							
782	23.8	42.0	.458	33.0	33.8	176	11.5
786	22.6	42.8	.758	31.4	37.0	189	12.1
868	23.9	42.3	.842	33.1	34.6	178	11.5
883	25.1	47.7	.633	34.2	36.7	211	12.1
884	24.1	43.3	.358	33.7	34.3	184	11.7
899	26.1	50.8	.683	36.5	37.6	228	12.3
902	25.5	50.5	.425	37.2	37.9	229	12.4
914	25.7	42.3	.733	30.9	32.0	168	10.9
914	26.0	47.5	.292	34.2	34.6	204	11.8
927	23.0	38.4	.483	31.3	32.1	154	11.0
928	24.3	39.9	.658	30.8	31.8	158	10.9
930	23.3	41.3	.425	33.2	34.0	174	11.5
936	23.3	41.1	.558	33.0	34.0	172	11.5
961	24.6	46.6	.742	35.5	36.8	205	12.1
974	24.5	46.2	.542	35.3	36.3	203	12.0
976	26.5	48.6	.525	34.4	35.3	210	11.8
984	25.4	47.8	.617	35.3	36.4	210	12.0
990	25.6	47.4	.675	34.7	35.8	206	11.9
1002	25.8	47.6	.608	34.6	35.5	206	11.9
1036	26.5	50.6	.583	35.7	36.7	224	12.1
1036	27.5	54.2	.642	37.0	38.0	245	12.4
1046	25.3	39.9	.708	29.6	30.6	153	10.5
1047	25.9	45.8	.533	33.2	34.0	193	11.5
1050	26.0	50.6	.642	36.5	37.6	227	12.3
1090	27.3	44.8	.850	30.8	32.0	178	10.9

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[161] For the detailed sources and analyses of these data, see Univ. Mo. Agr. Exp. Sta. Res. Bulls. 222, 1935, 238 and 239, 1936.

TABLE 21.7. *Continued.*

Average Live wt., lbs.	Feed TDN, lbs./day	Milk FCM, lbs./day	Live wt. gain, lbs./day	Gross Energetic Effic.		Profit per year, dollars*	
				Not corrected for wt. gain	Corrected for wt. gain	per cow	per 1000 lbs. FCM
Shorthorns, 28							
1014	19.9	33.6	.775	31.7	33.2	136	11.1
1093	16.1	21.1	1.167	24.5	26.8	66	8.6
1094	18.9	38.5	.625	38.4	39.8	178	12.7
1100	21.3	43.4	1.158	38.2	40.9	200	12.7
1146	22.5	32.4	1.067	27.0	28.6	113	9.6
1172	19.6	34.8	1.092	33.3	35.7	147	11.6
1184	20.2	37.5	.725	34.9	36.4	164	11.9
1186	20.1	35.4	.942	33.0	35.0	148	11.6
1196	21.7	33.5	1.050	28.9	30.7	126	10.3
1206	19.2	33.0	1.067	32.3	34.6	136	11.3
1214	20.1	24.0	1.525	22.4	24.6	65	7.4
1214	20.6	31.4	.992	28.5	30.2	116	10.1
1223	17.6	26.9	.100	28.6	28.8	100	10.1
1226	22.2	32.5	1.058	27.5	29.1	116	9.8
1230	21.4	32.6	.950	28.5	30.0	120	10.1
1286	18.8	27.9	.667	27.8	29.0	101	9.9
1289	19.9	33.7	.383	31.8	32.6	137	11.1
1297	23.4	31.6	.917	25.2	26.5	102	8.8
1306	20.5	33.0	1.058	30.2	32.2	129	10.7
1314	20.9	32.8	.817	29.4	30.8	125	10.4
1326	18.7	35.4	.342	35.5	36.3	156	12.0
1329	20.9	21.1	1.950	19.0	21.4	40	5.1
1380	23.9	34.7	1.192	27.2	28.9	122	9.7
1386	20.8	29.0	.825	26.0	27.3	97	9.2
1398	25.6	40.6	.642	29.7	30.6	156	10.6
1405	22.8	35.9	.850	29.4	30.8	137	10.4
1408	20.6	30.7	.667	27.9	29.1	111	9.9
1442	21.3	34.8	1.158	30.6	32.8	137	10.8
Dixon, Illinois, Testing Plant Holsteins, 42							
889	26.6	43.6	.370	30.7	30.8	172	10.8
952	25.1	43.7	.192	32.6	32.7	181	11.3
976	25.9	38.7	−.110	28.0	28.0	141	10.0
1086	23.2	41.3	.520	33.4	33.7	175	11.6
1126	26.4	47.0	.358	33.3	33.5	198	11.5
1161	27.7	52.5	.233	35.5	35.6	231	12.0
1194	26.4	42.7	−.356	30.3	30.2	167	10.7
1198	29.9	67.2	.096	42.1	42.2	327	13.3
1210	28.6	67.8	.110	44.4	44.4	338	13.6
1211	26.6	43.0	.000	30.3	30.3	168	10.7
1220	30.0	61.4	.000	38.4	38.4	284	12.7
1221	27.3	41.0	.559	28.1	28.3	150	10.0
1229	28.0	53.5	−.301	35.9	35.7	237	12.1
1233	29.4	47.0	−.301	33.2	33.3	182	10.6
1245	28.1	50.2	−.068	33.4	33.4	212	11.6
1247	27.1	44.7	.206	30.9	31.0	178	10.9
1265	28.3	55.3	.274	36.6	36.7	249	12.3
1271	29.0	55.6	.247	36.0	36.1	247	12.2
1272	28.8	52.5	−.333	34.2	34.1	226	11.8
1291	26.9	53.8	−.329	37.5	37.3	246	12.5
1297	27.3	50.9	.301	35.0	35.1	222	12.0
1312	28.2	43.9	−.274	29.2	29.1	166	10.4
1330	28.5	53.2	.000	35.1	35.1	233	12.0
1331	25.8	45.6	.315	33.1	33.2	192	11.5
1340	26.1	53.4	−1.041	38.4	37.8	247	12.7
1347	27.8	59.9	.109	40.5	40.5	286	13.1
1350	25.5	41.9	.247	30.8	30.9	166	10.8
1354	27.1	54.2	.055	37.5	37.5	248	12.5
1358	29.2	56.8	−.192	36.4	36.4	255	12.3
1360	29.5	56.8	.041	36.1	36.1	253	12.2
1425	26.1	42.6	.137	30.5	30.6	168	10.8
1448	30.1	56.7	−.269	35.2	35.1	248	12.0
Dixon, Illinois, Testing Plant Holsteins, 42 cows—*Continued*							
1464	27.6	46.9	.167	31.8	31.9	191	11.2
1469	30.8	64.6	−.110	39.3	39.3	303	12.8
1514	28.6	57.3	−.055	37.5	37.5	261	12.5
1531	23.8	36.4	.548	28.7	28.9	136	10.2
1538	29.0	53.0	.055	34.3	34.3	228	11.8
1566	28.7	56.3	.205	36.7	36.8	254	12.4
1609	30.3	50.3	.208	31.1	31.1	201	11.0
1660	28.0	40.0	.192	26.8	26.8	138	9.4
1683	29.4	61.4	.137	39.1	39.2	287	12.8
1748	31.9	58.4	.274	34.3	34.4	251	11.8
Pennsylvania (Forbes) Holsteins, 10							
867	16.0	32.5	−.056	38.0	37.8	149	12.6
1008	16.6	30.6	.036	34.7	34.7	132	11.8
1042	20.0	39.7	.259	37.3	38.0	181	12.5
1073	18.9	36.1	.205	35.8	36.4	160	12.1
1092	19.8	35.5	−.056	33.7	33.5	151	11.6
1102	20.6	34.6	.652	31.5	33.0	140	11.1
1198	21.6	39.4	.580	34.3	35.7	169	11.8
1207	19.1	34.9	.154	34.3	34.6	150	11.8
1308	20.7	33.6	.542	30.5	31.7	132	10.8
1408	24.4	45.1	−.165	34.7	34.3	195	11.8
Savage's Guernseys, 2							
846	16.0	24.4	.200	28.5	29.3	90	10.1
1072	19.3	32.7	.514	31.8	33.8	134	11.2
Savage's Holsteins, 14							
985	21.2	35.8	.695	31.7	34.0	145	11.1
990	21.2	36.9	.086	32.6	32.9	153	11.4
1035	20.9	29.7	.838	26.6	29.1	102	9.4
1053	22.9	42.5	.295	34.9	35.9	185	11.9
1054	20.2	29.9	.029	27.8	27.9	108	9.9
1073	20.8	30.4	.162	27.3	27.8	108	9.7
1090	22.7	37.7	.657	31.1	33.2	151	11.0
1150	21.7	38.5	.638	33.3	35.5	162	11.5
1175	21.4	32.4	.581	28.4	30.1	119	10.1
1179	22.7	37.5	.019	30.9	31.0	149	10.9
1184	24.4	40.6	.209	31.2	31.8	163	11.0
1239	23.8	40.2	.419	31.6	32.8	163	11.1
1253	23.4	38.2	.752	30.7	29.4	151	10.8
1341	22.1	30.1	.438	25.5	26.6	99	9.0
Savage's Jerseys, 6							
812	18.8	34.7	.009	34.5	34.6	150	11.9
860	17.0	26.4	.095	29.2	29.6	101	10.4
865	17.9	34.4	.248	36.1	35.1	154	12.3
909	17.6	23.4	.505	25.0	26.6	75	8.7
925	16.6	24.7	.571	27.8	30.0	89	9.9
931	19.7	32.8	.752	30.7	33.4	128	10.8
Perkins' Holsteins, 4							
1288	22.0	28.6	.336	24.4	25.2	88	8.5
1330	22.0	28.2	.781	24.0	26.0	85	8.3
1360	18.3	24.8	.432	25.3	26.7	80	8.9
1393	21.4	27.8	.371	24.4	25.4	86	8.5

TABLE 21.7 *Continued.*

Average Live wt., lbs.	Feed TDN, lbs./day	Milk FCM, lbs./day	Live wt. gain, lbs./day	Gross Energetic Effic.		Profit per year, dollars*	
				Not corrected for wt. gain	Corrected for wt. gain	per cow	per 1000 lbs. FCM
Haecker's Guernseys, 16							
765	12.6	16.6	.196	24.6	25.4	52	8.6
766	13.8	22.7	.050	30.7	30.9	90	10.9
782	12.5	21.9	.102	32.8	33.4	91	11.4
790	13.8	24.7	.008	27.6	27.6	84	9.8
801	12.4	22.7	−.133	34.3	33.5	98	11.8
840	17.2	29.8	.029	32.5	33.7	124	11.4
843	13.5	27.0	−.240	37.4	36.0	123	12.5
855	15.9	23.4	.008	27.6	27.6	84	9.8
864	17.9	30.3	−.109	33.6	33.1	129	11.6
887	14.0	29.7	−.488	39.8	37.0	140	12.9
909	18.0	32.8	−.082	34.2	33.9	141	11.8
925	15.1	22.3	−.060	27.7	27.4	80	9.8
947	15.3	20.1	−.095	24.7	24.4	63	8.6
996	15.8	21.1	.103	25.0	25.4	67	8.7
998	20.5	37.6	−.191	34.3	33.7	162	11.8
1019	17.4	26.3	.143	28.4	28.9	97	10.1
Haecker's Holsteins, 27							
781	15.1	22.5	.077	27.9	28.2	82	10.0
817	14.1	22.7	.095	30.1	30.5	88	10.6
844	14.6	29.6	−.429	38.0	35.8	136	12.6
872	16.0	17.3	.165	20.3	20.7	39	6.2
877	17.4	29.4	−.089	31.7	31.4	119	11.1
880	16.9	35.2	.050	39.1	39.4	164	12.8
887	13.4	30.2	.278	42.1	40.3	147	13.4
888	14.8	28.6	−.230	36.1	35.0	127	12.2
890	18.3	37.8	−.319	38.7	37.3	176	12.7
906	17.5	32.2	−.071	35.5	35.2	139	11.8
919	16.2	27.8	−.214	32.1	31.2	114	11.2
923	16.5	31.4	−.286	35.8	34.5	139	12.1
975	16.4	23.5	.191	26.9	27.6	82	9.6
976	18.8	26.6	.223	26.6	27.2	92	9.4
978	19.2	32.3	−.196	31.6	30.9	131	11.1
985	19.9	37.0	−.120	34.9	34.4	161	11.9
1086	18.8	27.7	.143	27.7	28.1	99	9.8
1095	18.4	29.8	−.042	30.2	30.2	117	10.7
1106	15.1	20.9	.226	25.9	26.7	70	9.2
1114	19.7	28.2	.161	26.8	27.3	98	9.5
1117	18.6	28.3	.113	28.4	28.8	104	10.0
1128	18.4	25.4	.238	25.9	26.6	85	9.2
1137	20.2	24.7	.226	22.9	23.4	70	7.7
1273	18.2	30.6	−.137	31.5	31.0	124	11.1
1292	19.7	36.1	.117	34.4	34.8	156	11.8
1298	20.1	30.4	.192	28.4	29.0	112	10.8
1315	18.6	31.8	.321	32.0	33.2	130	11.2
Haecker's Jerseys, 55							
634	14.4	28.5	−.137	36.9	36.2	129	12.4
683	11.1	18.6	−.053	31.5	31.2	75	11.0
706	14.7	25.5	−.286	32.6	31.3	106	11.4
734	12.5	27.5	−.010	41.2	41.4	132	13.2
735	12.6	20.8	−.034	31.0	31.2	83	10.9
735	14.6	22.6	.238	28.9	30.0	85	10.3
752	12.8	21.8	−.060	31.8	31.5	89	11.2
752	14.2	22.8	.006	30.1	30.1	89	10.7
754	13.8	23.5	−.027	31.9	31.8	96	11.2
758	15.1	27.6	−.114	34.1	33.6	119	11.8
760	11.8	16.3	.008	26.0	26.0	55	9.2
778	13.1	31.6	−.893	45.2	39.5	159	13.8
782	15.9	28.8	.137	33.9	34.6	123	11.7
783	12.5	19.4	−.080	29.0	28.6	67	9.5
789	13.4	24.1	.202	33.6	34.7	102	11.6
792	14.5	27.8	−.398	35.9	33.9	123	12.1
793	14.2	23.6	.115	31.0	31.6	94	10.9
796	12.5	25.5	−.092	38.1	37.5	118	12.7
800	14.1	28.6	−.095	38.0	37.4	131	12.6
Haecker's Jerseys, 55 *Continued*							
809	14.2	30.9	−.414	40.9	38.5	148	13.1
809	15.3	25.4	.048	31.1	31.3	102	11.6
811	13.8	24.1	−.333	32.8	31.2	100	11.4
811	15.3	29.4	−.184	36.0	35.1	131	12.2
817	12.7	25.6	−.364	37.7	35.6	117	12.5
817	13.7	27.0	−.060	36.9	36.5	122	12.4
820	14.0	22.5	.113	30.3	30.8	88	10.7
820	15.1	18.5	.196	23.0	23.6	52	7.8
824	16.6	26.7	−.036	30.1	30.0	104	10.7
833	16.2	30.0	−.161	34.7	34.0	131	12.0
836	14.0	28.4	−.143	38.1	37.3	131	12.6
838	13.6	26.2	−.097	36.2	35.7	117	12.2
843	14.9	21.1	.143	26.4	27.0	72	9.4
845	13.6	23.2	−.010	31.9	31.8	94	11.1
849	16.8	30.1	−.225	33.5	32.6	128	11.6
854	14.5	21.1	.017	27.3	27.3	75	9.8
855	16.0	29.2	−.025	34.2	34.1	126	11.8
856	15.3	23.5	−.080	28.8	28.5	88	10.2
858	13.4	23.1	−.500	32.3	30.0	95	11.3
859	12.3	26.0	−.311	39.6	37.6	122	12.9
861	14.8	24.3	.101	30.7	31.2	96	10.8
863	15.0	24.6	.018	30.9	30.8	98	10.9
867	14.7	25.6	−.214	32.7	31.8	107	11.4
876	13.8	24.0	−.082	32.5	32.1	99	11.3
887	15.4	22.0	−.103	26.8	26.4	76	9.4
890	15.2	23.0	.071	28.5	28.8	85	10.1
898	14.8	23.8	−.131	30.1	29.6	93	10.7
902	16.2	30.9	−.036	35.6	35.5	136	12.1
910	18.6	37.0	.024	37.1	37.2	168	12.5
915	13.7	18.0	.036	24.6	24.7	56	8.5
935	17.6	31.3	−.074	33.3	33.0	132	11.5
936	18.6	28.8	−.113	28.9	28.6	108	10.3
989	15.9	26.1	.250	30.7	31.8	103	10.8
1013	15.8	23.2	−.009	27.5	27.4	83	9.8
1046	14.3	20.4	.148	26.8	27.4	71	9.5
1071	13.0	15.4	.077	22.1	22.4	41	7.3
Eckles' Holsteins, 2							
1056	20.0	34.3	.000	32.1	32.1	140	11.2
1319	18.1	29.9	.019	30.9	29.9	119	10.9
Eckles' Jerseys, 5							
807	15.5	24.8	.041	30.0	30.1	96	10.6
824	14.9	22.8	.137	28.6	29.2	84	10.1
899	16.4	28.6	.044	32.7	32.9	119	11.4
902	9.2	10.5	.049	21.3	21.5	26	6.8
952	15.0	21.7	.000	27.1	27.1	76	9.6
Hills' Holsteins, 4							
1184	11.2	9.4	.487	15.7	17.3	7	2.0
1317	17.2	20.7	.752	22.5	23.4	57	7.5
1341	16.2	11.4	.893	13.2	14.9	−5	−1.3
1390	18.4	20.5	.307	20.9	21.6	49	6.6
Hills' Jerseys, 5							
885	14.0	17.9	.627	24.0	26.6	54	8.3
899	14.2	19.4	.548	25.6	27.9	64	9.0
920	15.2	17.2	.613	21.1	22.8	42	6.7
929	16.6	19.4	.410	22.0	23.2	51	7.3
978	13.7	13.6	.458	18.6	20.0	24	4.9

TABLE 21.7 *Continued*

Average Live wt., lbs.	Feed TDN, lbs./day	Milk FCM, lbs./day	Live wt. gain, lbs./day	Gross Energetic Effic.		Profit per year, dollars*	
				Not corrected for wt. gain	Corrected for wt. gain	per cow	per 1000 lbs. FCM
Harrison and Savage's Holsteins, 103							
1081	19.4	34.5	.155	33.4	33.9	146	11.6
1120	16.2	22.2	.192	25.6	26.3	73	9.0
1134	19.6	32.8	.075	31.4	31.7	132	11.0
1138	18.9	31.3	.367	31.1	32.5	125	10.9
1154	20.0	32.8	−.150	30.8	30.3	130	10.8
1159	16.5	24.4	.425	27.7	29.3	87	9.8
1162	18.9	28.4	−.376	28.2	27.1	104	10.0
1163	18.9	28.1	.214	27.8	28.5	102	10.0
1170	19.2	30.7	.711	28.9	31.3	119	10.6
1170	23.1	43.2	.169	35.1	35.6	189	12.0
1172	17.4	22.7	.432	24.4	25.7	70	8.5
1173	20.5	34.3	−.316	31.4	30.4	138	11.0
1181	16.6	20.1	.335	22.7	23.7	56	7.6
1182	18.8	29.6	−.078	29.7	29.4	115	10.6
1184	22.2	41.9	.171	35.4	36.0	184	12.0
1187	18.4	25.9	.244	26.4	27.2	88	9.3
1192	18.6	29.3	.004	29.5	29.6	112	10.5
1195	22.0	41.0	.120	35.0	35.4	179	12.0
1195	22.3	41.0	−.026	34.5	34.4	177	11.8
1196	16.6	19.1	.120	21.6	21.9	49	7.0
1203	21.7	39.4	−.030	34.0	23.9	169	11.8
1203	18.1	23.3	.530	24.1	25.7	71	8.3
1210	18.2	27.2	.150	28.0	28.5	99	10.0
1215	19.6	31.6	.398	30.1	31.5	123	10.7
1217	19.3	28.4	.384	27.6	28.8	101	9.8
1219	20.9	34.0	−.184	30.5	29.9	134	10.8
1220	16.9	22.6	.756	25.0	27.6	72	8.8
1220	16.1	23.4	.004	27.2	27.2	82	9.6
1223	16.8	26.8	.188	30.0	30.8	139	11.4
1224	19.1	28.0	1.053	27.5	31.1	100	9.8
1227	17.9	26.4	−.489	27.7	26.1	95	9.8
1230	16.8	23.4	.249	26.1	26.9	78	9.2
1232	20.4	33.2	.087	30.5	30.7	130	10.7
1234	16.2	25.1	−.200	29.1	28.4	95	10.4
1238	18.3	26.4	−.278	27.0	26.2	92	9.6
1239	20.0	38.2	.074	35.7	36.0	169	12.1
1239	19.7	28.7	.192	27.4	28.0	102	9.7
1248	18.9	26.5	.466	26.3	27.8	90	9.3
1250	19.7	31.6	.188	30.1	30.7	123	10.7
1251	19.4	32.3	−.278	31.2	30.3	130	11.0
1251	19.0	27.1	.015	26.7	26.7	94	9.5
1254	19.5	31.6	−.188	30.3	29.7	123	10.7
1255	18.2	29.6	−.049	30.4	30.2	116	10.7
1261	20.9	36.0	.155	32.4	32.9	149	11.3
1266	17.7	23.7	.282	25.1	25.9	76	8.8
1267	19.6	31.2	.455	29.9	31.5	121	10.6
1270	20.4	33.8	−.116	31.0	30.6	134	11.0
1271	18.7	27.2	.587	27.4	29.3	97	9.7
1272	17.4	20.6	.327	22.2	23.1	55	7.3
1272	18.6	30.5	.098	30.7	31.1	121	10.9
1272	20.8	34.9	.216	31.4	32.1	141	11.1
1275	20.1	29.2	.470	27.2	28.6	103	9.6
1275	20.7	34.6	.443	31.3	32.8	139	11.0
1283	17.5	22.8	.244	24.3	25.1	70	8.5
1285	20.4	32.8	.229	30.1	30.8	128	10.7
1286	17.9	23.2	.105	24.3	24.6	71	8.4
1287	19.7	31.9	.169	30.3	30.9	125	10.7
1292	20.7	35.1	.045	31.8	32.0	143	11.2
1295	19.5	30.4	.263	29.2	30.0	115	10.4
1296	19.1	26.5	.131	26.0	26.4	89	9.2
1297	20.7	32.6	.470	29.5	31.0	125	10.5
1298	20.4	34.9	.613	32.1	34.3	143	11.2
1298	21.0	36.4	.065	32.5	32.7	150	11.4
1301	21.5	39.2	.090	34.1	34.4	168	11.8
1305	20.8	32.4	.384	29.2	30.4	123	10.4
1306	18.5	27.8	.511	28.1	29.9	101	12.7
1308	17.5	22.7	.756	24.3	26.8	70	9.4
1320	19.6	30.8	.131	29.4	29.8	117	10.4
1323	19.7	33.9	.176	32.3	32.9	140	11.3
1323	20.6	32.3	.214	29.3	30.0	123	10.4
1327	20.8	34.1	.128	30.7	31.1	135	10.8
1327	17.6	22.8	.150	24.3	24.7	70	8.4
1331	21.7	39.7	−.237	34.3	33.5	171	11.8
1332	17.3	19.8	−.011	21.4	21.4	50	6.9
1332	17.9	20.2	.688	21.2	23.1	50	6.7
1333	21.5	35.6	.261	31.1	31.9	143	11.1
1337	19.4	33.5	.351	32.5	33.8	139	11.4
1338	20.8	35.3	.004	31.8	31.8	144	11.2
1340	18.7	26.1	−.045	26.1	26.0	88	9.2
1340	18.0	32.8	.327	34.1	35.4	140	11.7
1341	20.0	33.4	.192	31.4	32.0	135	11.1
1344	18.1	22.0	.853	22.8	25.3	61	7.6
1344	18.8	33.8	−.331	32.8	31.6	137	11.4
1346	21.0	33.8	.343	29.4	30.4	125	10.4
1364	18.4	26.6	.421	27.1	28.5	94	9.7
1366	19.5	27.6	.518	26.6	28.2	95	9.4
1368	18.9	33.5	.053	32.3	32.5	134	10.3
1375	19.3	29.2	.004	28.4	28.4	107	10.0
1379	19.1	30.6	.147	30.0	29.5	119	10.7
1379	19.6	33.9	−.131	32.4	31.9	140	11.3
1382	18.6	22.8	.150	24.3	24.7	70	8.4
1384	20.9	33.3	.286	29.9	30.8	129	10.6
1386	21.3	41.0	.016	36.1	36.1	183	12.2
1388	21.8	38.8	.265	33.3	34.2	164	11.6
1389	19.9	31.7	.447	29.9	31.4	123	10.6
1394	21.3	40.1	−.690	35.3	33.0	176	12.1
1398	20.9	35.1	.271	31.5	32.4	142	11.1
1404	15.8	22.9	.637	27.1	29.6	80	9.6
1428	19.2	28.6	−.387	27.9	26.8	104	10.0
1436	19.2	28.6	.082	27.8	28.1	103	9.9
1453	18.4	27.4	.494	27.9	29.5	99	9.4
1494	21.5	38.7	−.327	33.8	32.7	165	11.5
1500	21.1	36.4	−.019	32.3	32.2	150	11.3

* Assuming that price of feed is $1.50 per 100 lbs. TDN; price of milk is $2.00 per 100 lbs. FCM.

TABLE 21.8. COMPOSITION OF COW BLOOD DURING FAST. MG/100 CC BLOOD

Days Fast	Lipin P	Total fatty acids	Sterol	Sterol Esters	Iron	Sugar	Amino Acid N	Inorganic P	Organic acid-soluble P	Ca	Cl
0	10.0	200	95	50	40	62	7	4	3	7	267
1½	10.4	214	96	37	43	65	7.1	4.9	2.4	7	261
2½	10.3		99	55	37	65	5.1	4.7	3.3	6.4	266
3½	10.1	224	96	58	44	45		4.9	3.2	6.8	279
4½	9.6	186	91	59		51	5.8	5.1	3.1	6.6	276
5½	9.5	201	88	48	41	52	6.2	4.9	3.0	6.4	280
6	9.4	204	88	46		52	6.1	4.6	2.6	6.8	276

Chapter 22

The Monetary Economy of Milk Production

> The dairy farmer would be very glad indeed to function more abundantly in the support of national health if an economic framework could be devised.
> *H. D. Kay*

The overall monetary economy of milk production—including cost of human labor—depends on many factors, of which the milk-production level per animal is most important. The latter may be raised by increasing (1) "dairy merit", (2) body size, and (3) plane of nutrition. We shall define and indicate the bearing of each on the monetary economy of milk production.

22.1: "Dairy merit": quantitative definition. The designation "dairy merit" is related to the economy of milk production, but the relation is not clear; it means different things to different dairymen. Let us, therefore, define it quantitatively by saying that "dairy merit" represents the biological efficiency of milk production as measured by the percentage of consumed *TDN* energy which is converted into milk (*FCM*) energy. This definition may be represented by the equation

$$\text{Dairy merit} = \frac{\text{milk-energy production}}{TDN\text{-energy consumption}} = \frac{340 \times \text{lb } FCM \text{ produced}}{1814 \times \text{lb } TDN \text{ consumed}} \qquad (1)$$

assuming that 1 lb *FCM* ("fat-corrected milk", milk containing 4 per cent fat) has an energy equivalent of 340 Calories, and 1 lb *TDN* (total digestible nutrients) has an energy equivalent of 1814 Calories. Dairy merit of the *animal* is numerically equal to the gross energetic efficiency of the lactation *process* (Chs. 1, 3, 21).

The upper limiting value of this dairy-merit ratio is 50 per cent; not over one-half of the consumed *TDN* energy can be converted into milk energy. Superior dairy animals convert about one-third of the consumed *TDN* energy into milk energy; good dairy animals, about one-fourth.[1] A 25 per cent dairy-merit level pays, approximately, for the dairyman's work, feed, and other expenses at the current rate. Really profitable milk production involves higher dairy merit.

The dairy merit, or efficiency, of a given animal is, of course, dependent on her milk-production level.

The average milk-production level in the United States is about 4500 lbs milk or 160 lbs butterfat per cow per year. This yield is about one-tenth of the upper lactational performance of cattle. A cow recently produced 42,000 lbs milk (about 1400 lb butte fat) in a year[2], and the writer believes, on the basis of considerations to be explaine presently, that the potential upper lactational performance for dairy cattle is neare 50,000 lbs *FCM* or 2,000 lbs butterfat a year.

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[1] Brody, S., *J. Nut.*, **17**, 235 (1939); *Science*, **95**, 485 (1942); Univ. Mo. Agr. Exp. Sta. Res. Bull. 366, 1943.

It is theoretically simple to double the average milk production of 4500 lbs milk, o 160 lbs butterfat a year by the use of well-bred sires. The simplicity is indicated in th following table.[3]

Sire used	Production, lbs/year					
	Original cows		First generation daughters		Second generation daughters	
	Milk	Fat	Milk	Fat	Milk	Fat
Guernsey	4,480	202	5,729	253	7,155	355
Holstein	3,631	176	6,649	278	10,218	395
Jersey	4,047	194	5,015	270	6,539	331
Average	4,110	192	5,815	267	8,056	363

The Dairy-Herd Improvement Association cattle currently produce from 8,000 t 10,000 lbs *FCM* (milk corrected to 4% fat) a year. The dairy cattle in Denmark produced, on the average, about 7500 lbs milk a year. On the other hand, the average productive level in Great Britain, Canada, and New Zealand is no better than in the Unite States, 4,000 to 5,000 lbs a year. These countries thus fail to make use of their dair potentialities. They could easily double the milk production with the same cattl population.

The dairy industry is evidently capable of great expansion in production and income easily doubling and potentially capable of tripling or quadrupling the present average production, without increasing the number of cows. The two outstanding needs are (1) a yardstick for *measuring dairy merit* of animals, *uncomplicated by differences in body* size; (2) a method for *predicting milking potentiality in young animals*. We attempted to correlate basal energy metabolism in the young with productive level in the adult. The difficulty in developing this, or any other, potentiality index is that it involves investigating large, unselected populations over many years, which is expensive. Just as methods have been developed for early recognition of intellectually gifted children,[4] so methods will be developed for early recognition of lactationally gifted cattle. The economic saving that may result from an index of lactational potentiality is indicated by the fact that of the 6 million dairy heifers raised annually, only one-third turn out to be profitable.

Dairy merit appears to be independent of body size *as such*; its upper limiting value is approximately the same in rats, goats, cows, and even in humans.

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[2] The 8-year old 1750-lb Carnation Ormsby Madcap Fayne, produced 41,943 lbs 3.33% fat milk in a (365-day) year [Prescott, M. S., *Holstein-Friesian World*, **39**, 679 (1942)]. This is equivalent to an average of 115 lbs milk a day (at one time she produced 146 lbs milk in a day; 19,508 quarts milk a year (1 qt = 2.15 lbs); 1740 lbs butter (1 lb butterfat = 1.25 lbs butter); 1463 lbs protein, equivalent to 3775 lbs American cheese; 2034 lbs lactose; 285 lbs minerals containing 58 lbs calcium, 37 lbs phosphorus, and so on. A the rate of 1 quart milk a day, this would supply one person for 53½ years. The 8 yea old 1700-lb cow Carnation Ormsby Butter King produced 38,607 lbs of 3.63% milk, 1402 lbs butterfat in a (365-day) year.

[3] McCandlish, A. C., *et al.*, Iowa Exp. Sta. Bull. 251.

[4] For early recognition of the intellectually gifted, see Terman, L. M., "Psychological approaches to the biography of genius." *Science*, **92**, 293 (1940).

Approximately the same percentage of digestible dietary nutrients consumed may be converted into milk in all these species, large or small.[5] The profit on milk production, however, does vary with body size of the animal because, if other conditions are equal, the overhead expense per unit milk production declines with increasing size of animal. Let us, therefore, next define body size quantitatively.

22.2: Lactationally effective body size: quantitative definition. Since the feed is converted into milk by the body, the quantity of such conversion should, other conditions being equal, increase with the size of the body. Body size must be an important factor. It is true that some large cows yield no more, and often less, than small ones; but this is because the *dairy merit*, the lactational drive, of the large cow is inferior to that of the small one—because other conditions are not equal. Thus dairy cows produce more milk than beef cows of the same size because of *dairy merit* differences. But when other conditions are equal, a small dairy cow should yield more milk than a dairy goat; a large dairy cow should yield more than a small dairy cow. Since there is a maintenance cost for every pound of live weight, each pound necessarily counts for or against the dairy merit and profit of the animal yielding a given quantity of milk energy, depending on whether or not each pound produces milk in proportion to its maintenance cost.

The major reason for the general neglect of the body weight datum in reporting milk yield is that milk production does not increase *directly* with *simple* body weight but in a more complex manner, which appears to be confusing. For instance, we know of a 700-lb cow (Stonehurst Patrician's Lily)[6] that produced at the rate of 70 lbs *FCM* a day, or 26,000 lbs *FCM* a year, but it is probably impossible for 1400-lb cow to produce at the rate of 140 lbs *FCM* a day or 52,000 lbs *FCM* a year. Milk production evidently does not increase directly with simple weight. This gives the superficial impression that body weight may not be an important factor in milk production, which is definitely not the case.

Milk is not produced by the body as a whole, but only by the visceral (internal) organs and by the surfaces that participate in the digestive, assimilatory, respiratory, excretory, and secretory (including endocrine) processes. The supporting structures (skeletal muscles and bones) do not participate in the milk-production process; and it so happens, for reasons previously explained (Ch. 17, also Ch. 13), that these non-participating supporting structures increase at a relatively more rapid rate, or the visceral and surface structures increase at a relatively less rapid rate, than the body as whole.

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[5] There is no reason for assuming that different amounts of consumed feed energy, *above the maintenance needs*, should be required to produce unit milk energy in, for example, 700 and 1400-lb cows; there is no reason why the energy cost of producing unit milk above the maintenance cost, should be different in the two animals. If the maintenance cost is included, the efficiency will be the same if the ratio of milk energy production to maintenance-energy cost is the same in large and small animals, and this appears to be the case.

[6] *Jersey Bulletin and Dairy World*, **54**, No. 15 (April 10, 1935).

In other words, a 1200-lb cow cannot produce ten-fold the milk energy of 120-lb goat at its upper limit, and a 1400-lb cow cannot produce twice th milk energy of a 700-lb cow at its upper limit, because large animals hav relatively larger supporting structures and, therefore, relatively smaller vis ceral organs and areas than small animals (Ch. 17).

In an analysis of milk-energy production in relation to body weight i different species[1] (rats, goats, and cows), milk production was observed t vary with, approximately, the 0.7 power of body weight, or $W^{0.7}$ (Fig. 22.1a This means that increasing body weight 1 per cent tends to cause an increas

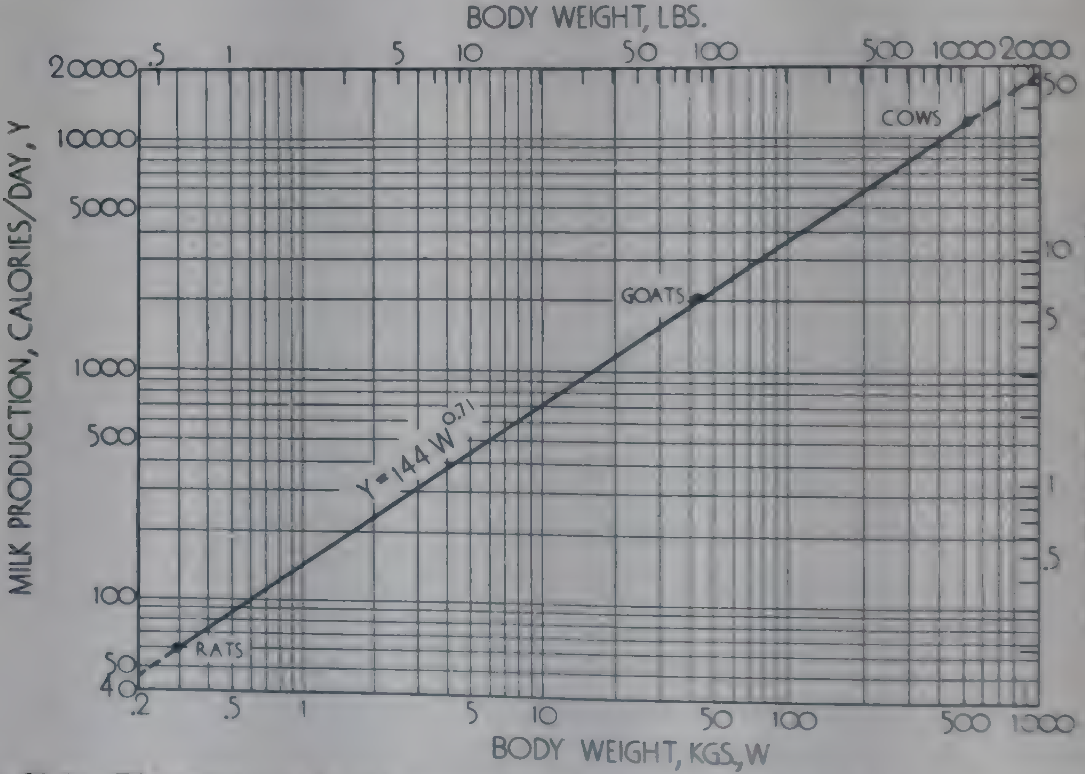

Fig. 22.1a. The relation of milk-energy production to body weight in mature animal of different species: averages of 368 "good" cows, 7 good goats, 5 excellent rat mothers Plotted on a logarithmic grid. Y represents milk-energy production per day for body weight, W.

in milk production of 0.7 per cent. More concretely, a 1400-lb cow tends t produce not 100 per cent more milk than a 700-lb cow, but only 70 per cen more, and this only when the dairy merits of the two cows are the same. Th reference base $W^{0.7}$ is, of course, very close to that of $W^{2/3}$, the conventiona reference base for the surface weight relation ($S = aW^{2/3}$); so that one ma say, if one prefers, that milk energy production tends to vary directly wit surface area.

Now, the basal energy metabolism and resting maintenance needs fo energy and protein also vary with, approximately, $W^{0.7}$ (Chs. 13–15). It i true that the energy cost of moving the body during walking and simila activities varies directly with body weight, with $W^{1.0}$, however, voluntar activities of animals tend to decline with increasing body weight; large animal are likely to make fewer and slower movements than small ones, and the decline appears to be in such manner that the total maintenance cost tends to vary with $W^{0.7}$, in the same manner as does milk-energy production (Ch. 15).

If, then, the maintenance-energy cost and the milk-energy production vary in the same manner with increasing body weight, dairy merit, *i.e.*, the ratio of milk-energy production to feed-energy consumption, must be the same in small and large animals[5] and this is virtually demonstrated for rats, goats, and cattle (Table 22.1). We thus reach the important conclusions that (1) if other conditions are equal, dairy merit is independent of body size; (2) milk-energy production, as maintenance cost, varies not with simple body weight, $W^{1.0}$, but with $W^{0.7}$. The *lactationally effective* body size is represented not by $W^{1.0}$ but by $W^{0.7}$.

Table 22.1. Milk Production in Relation to Various Reference Bases in Cattle, Goats, and Rats

	Average of 368 "good" cows	Average of 7 "good" goats	Average of 12 "good" white rats	A "champion" Holstein cow[1]	A "champion" Jersey cow[2]
Live weight, (lbs)	1,130	95	0.662	1,700	700
Live weight, (kg)	513	43	0.3	771	318
Milk yield, *FCM* (lbs/day)	33.6	6.2	0.1765	100	71
Milk yield, (Cal/day)	11,440	2,114	60	34,000	24,140
Ratio *FCM* lbs per 1000 lbs live wt.	30	66	267	59	101
Ratio milk Cal per kg live weight	22	50	150	44	63
Ratio Milk Cal to estimated basal-met. Cal	1.7	1.9	2.1	3.8	5.1
Milk Cal per $kg^{0.70}$ live weight[3]	145	152	139	324	428
Milk Cal per $kg^{0.73}$ live weight[4]	120	137	147	266	360
Ratio *FCM* lbs to $lb^{0.7}$ live weight[5]	24.5	25.6	23.6	54.8	72.4
Dairy merit = gross energetic efficiency[6]	31%	34.9%	44%	44%	48%

[1] This 1700-lb cow, Carnation Ormsby Butter King "Daisy" [*Holstein-Friesian World*, **33** (Feb. 22, 1936)] produced in 365 days 38,607 lbs of 3.63%-fat milk containing 1402 lbs butterfat.

[2] This 700-lb cow, Stonehurst Patrician's Lily [*Jersey Bull. & Dairy World*, **54**, No. 15 (April 10, 1935)] produced in 365 days 24,094 lbs of 4.5%-fat milk containing 1087 lbs butterfat.

[3] The $kg^{0.70}$ values are respectively: 78.9, 13.9, 0.4305, 105, 56.5.

[4] The $kg^{0.73}$ values are respectively: 95.1, 15.6, 0.4152, 128.1, 67.1.

[5] The $lb^{0.7}$ values are respectively: 137.1, 24.2, 0.7492, 182.5, 98.1.

[6] Dairy merit of a 120-lb goat is 44% when producing 15 lb *FCM*/day; 47.5% when producing 20 lbs/day; 41% when producing 12 lbs *FCM*, 39% for 10 lbs, 40.5% for 11.2 lbs.

22.3: Evaluation of dairy merit. *Dairy merit* is defined by the ratio of milk-energy production to *TDN*-energy consumption. It is easy to obtain the milk-energy production[7] but difficult to obtain the *TDN*-energy consumption. Because of this difficulty indirect dairy-merit *indices* may be used.

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[7] Milk-energy production (according to Gaines) = 340 x lb *FCM*. *FCM* represents milk corrected to 4% fat. Table 22.3 lists factors and equations for converting milk of any fat percentage to *FCM*.

The dairy-merit index proposed by Gaines[8] is the ratio of milk production to live weight, FCM/W, as for example, milk production per 1000 lb live weight.

The FCM/W dairy-merit index is the easiest to compute and to understand. It is, perhaps, satisfactory for comparing animals of nearly the same body weight, such as those within a homogeneous breed of cattle. But the FCM/W index is not satisfactory when animals differ widely in weight, as, for example, Carnation Ormsby Butter King Daisy and Stonehurst Patricians Lily (1700 lbs and 700 lbs, respectively). The 700-lb cow produced at the average rate of 70 lbs FCM a day, while it is probably physically impossible for a 1700-lb cow to produce $70 \times \frac{1700}{700} = 170$ lbs FCM a day.

The first three columns in Table 22.1 show that the ratio of milk Calories to simple body weight, kg, declines from 150 for rats to 50 for goats to 22 for cows; the FCM lbs per 1000 lbs body weight ratio declines from 267 for rats, to 66 for goats, to 30 for cows. On the other hand, the ratio of FCM lbs to $(\mathrm{lb})^{0.7}$ body weight is virtually the same, about 25 for rats, goats, and cows. The ratio of milk Cal. to basal metabolism Cal. is also quite constant, 2.1 for rats, 1.9 for goats, 1.7 for cows. The ratios of milk Cal. to $(\mathrm{kg})^{0.70}$, and to $(\mathrm{kg})^{0.73}$ are also quite constant.

The two right-hand columns in this table show, as might be expected, that the ratios of milk energy to estimated basal metabolism, or to $(\mathrm{kg})^{0.7}$ in the "champion" cows, are much above that for the "good" cows, about threefold in the champion Jersey. The ratio of milk-energy to $(\mathrm{kg})^{0.7}$ is likewise three times as high in the champion Jersey as in the "good" cows.

Incidentally, Gaines' FCM/W dairy-merit index indicates that the champion Jersey is about 70 per cent "better" than the champion Holstein (101:59); the milk Cal/$(\mathrm{kg})^{0.71}$ index indicates that the champion Jersey is about 33 per cent "better" than the champion Holstein (404:303); by the milk Cal/basal metabolism Cal. method, the champion Jersey is likewise about 33 per cent "better" than the Holstein (5.1:3.7).

According to equation (3) below, a 1700-lb cow producing 138 lbs FCM a day should have the same dairy merit or milk-producing efficiency as a 700-lb cow producing 70 lbs FCM a day. Actually, as shown in Table 22.1, the 1700-lb cow produced only 100 lbs FCM a day. The 1700-lb cow producing 100 lbs FCM a day is thus inferior, from the dairy-merit viewpoint, to the 700-lb cow producing 70 lbs FCM a day.

Summarizing, if the range in live weight of animals is considerable, the *relative* dairy merit of the animals under comparison is best given by the ratio $FCM/W^{0.7}$ or, perhaps, $FCM/W^{0.73}$, or best, by the dairy merit, that is the percentage TDN converted into milk (Table 22.2). The method of computing these values will be presently explained.

If milk-energy production tends to vary with $W^{0.7}$, how does it happen that Gaines reported that FCM tends to vary more nearly with $W^{1.0}$? A clue to this puzzle is given in Figs. 22.1b and c, which represent the same data on logarithmic and arithmetic grids, respectively.

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[8] Gaines, W. L., *J. Dairy Sci.*, **23**, 71, 259, 1031 (1940), and references there given. Gaines suggested the use of a special weight, the initial weight, I. W., at the beginning of the lactation period, shortly after freshening.

The slopes of the curves in the two charts (the slopes represent the exponents of W, the value of b in W^b) range from 0.3 for well-fed animals of almost exactly the same age to 1.3 and 2.1 for animals including all ages and all states of nutrition, animals classified by live weight regardless of age and state of nutrition. These differences in slope for the various cow populations thus reflect differences in the composition of the population.

If animals different in age are included in the population classified by weight (regardless of age), the increase in milk production associated with increased body weight is fortified by increase in milk production associated with increasing age during growth.

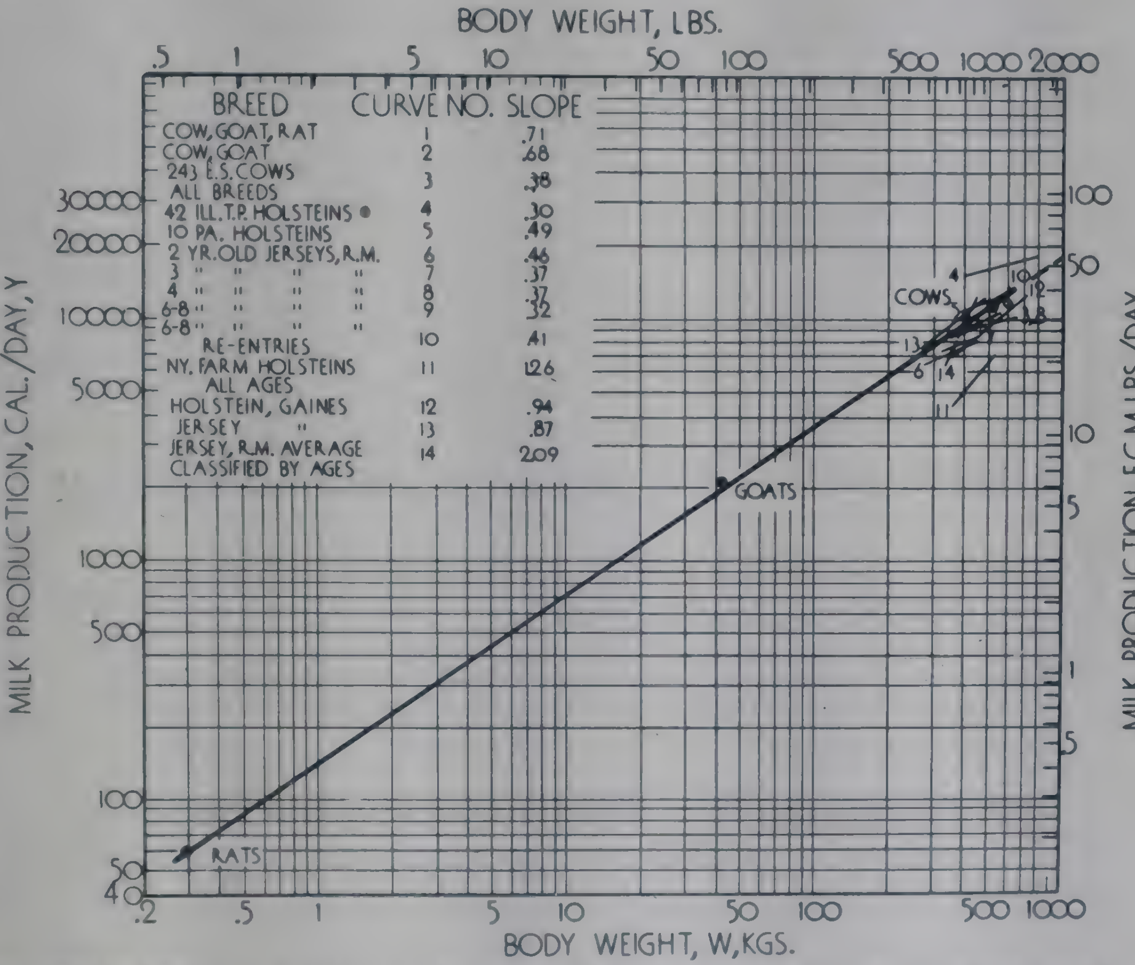

Fig. 22.1b Milk production as function of body weight on a logarithmic grid. The heavy line represents mature rats, goats, and the 368 "good" cows of all breeds, and has a slope of 0.71 (i.e. $Y = aW^{0.71}$). The other curves represent various groups of cows as shown. Note the wide variations in the slopes of the cattle data due to differences in grouping by ages, nutritional status, and dairy merit.

If animals in different nutritional conditions are included, increase in weight as result of fattening will not increase milk production; on the other hand, if undernourished animals are included, the light animals may have a lower yield than they should and when mixed with well-fed animals will give the curve a greater slope.

Summarizing, unless the cow population is homogeneous with regard to age, state of nutrition, and dairy merit, the slope relating milk yield to body weight is ambiguous. Thus curve 14 (Figs. 22.1b and c) of very high slope represents the same data as curves 2 to 10, each of low slope. Curves 14 and 11 have high slopes because they have animals of different ages, and so on. The differences in slope reflect differences in classification of data.

Instead of employing dairy-merit *indices*, such as $FCM/W^{0.7}$ or $FCM/W^{0.73}$ which are numerically removed from the actual values of *dairy merit*, a tabl or graph may be constructed giving dairy-merit estimates, estimates of th percentages of consumed *TDN* energy that is converted into milk energy

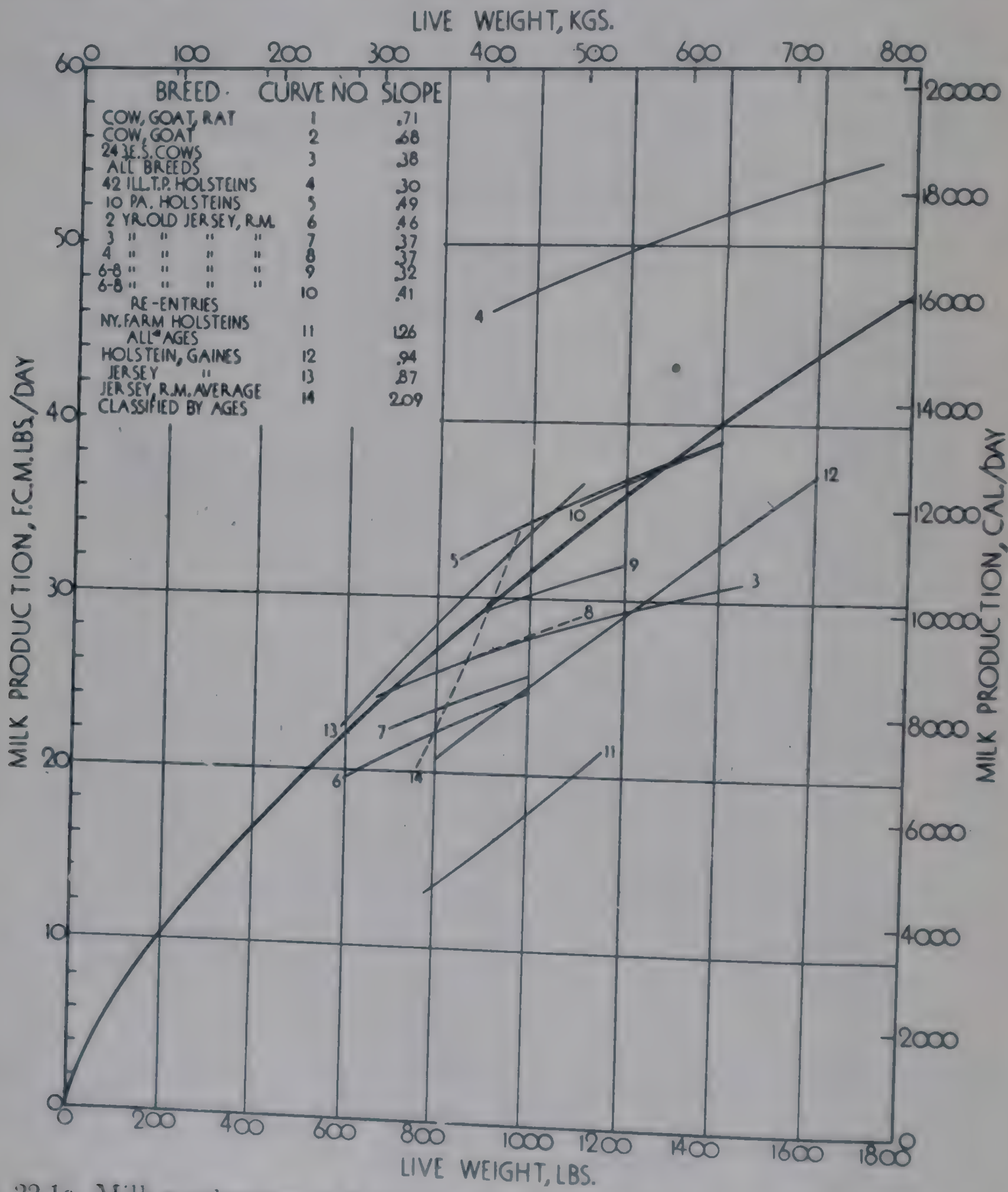

Fig. 22.1c. Milk production as function of body weight on an arithmetic grid The same data as in Fig. 22.1b. The longest heavy line represents the mature rats, goats. and 368 cows ($Y = aW^{0.71}$). The other curves are numbered as in Fig. 22.1b.

Such are Table 22.2 and Fig. 22.2. This table and alignment chart were constructed from the following considerations.

From the preceding chapter, the partition of *TDN* between milk (*FCM*) productior and maintenance is given by the relation

$$TDN = 0.305FCM + 0.053W^{0.73} \tag{1}$$

Table 22.2. Estimating Per Cent Efficiency of Milk Production from Body Weight of Cow and Milk Production (4% Milk)

4% milk, pounds per year. (FCM)	Body Weight, Pounds													4% milk, pounds per day
	600	700	800	900	1000	1100	1200	1300	1400	1500	1600	1700	1800	
3000	18.9	17.4	16.2	15.2	14.4	13.6	13.0	12.4	11.8	11.4	10.9	10.6	10.2	8.2
3500	21.0	19.5	18.2	17.1	16.1	15.3	14.6	14.0	13.4	12.9	12.4	12.0	11.6	9.6
4000	22.9	21.2	19.9	18.7	17.8	16.9	16.2	15.5	14.8	14.3	13.8	13.3	12.9	11.0
4500	24.6	22.9	21.6	20.4	19.3	18.4	17.6	16.9	16.2	15.6	15.1	14.6	14.1	12.3
5000	26.1	24.6	23.1	21.7	20.8	19.9	18.9	18.2	17.5	16.9	16.3	15.8	15.3	13.7
5500	27.6	25.9	24.4	23.2	22.1	21.0	20.2	19.5	18.7	18.1	17.5	17.4	16.4	15.1
6000	28.9	27.2	25.7	24.4	23.2	22.3	21.5	20.6	19.9	19.1	18.6	18.0	17.5	16.4
6500	30.2	28.3	26.8	25.7	24.6	23.4	22.5	21.7	21.0	20.2	19.7	19.1	18.5	17.8
7000	31.3	29.6	28.1	26.8	25.5	24.6	23.6	22.9	21.9	21.4	20.6	20.1	19.5	19.2
7500	32.2	30.6	29.1	27.7	26.6	25.5	24.6	23.8	23.0	22.3	21.6	21.0	20.4	20.5
8000	33.4	31.5	30.2	28.7	27.7	26.6	25.5	24.7	24.0	23.2	22.5	21.9	21.4	21.9
8500	34.3	32.6	31.1	29.6	28.5	27.4	26.4	25.7	24.7	24.0	23.4	22.7	22.1	23.3
9000	35.0	33.4	31.9	30.6	29.4	28.3	27.4	26.4	25.7	24.9	24.2	23.6	23.0	24.7
9500	35.8	34.1	32.8	31.3	30.2	29.2	28.1	27.4	26.4	25.7	25.1	24.4	23.8	26.0
10000	36.7	34.9	33.5	32.2	30.9	30.0	29.1	28.1	27.2	26.4	25.9	25.1	24.6	27.4
10500	37.3	35.6	34.2	33.0	31.7	30.7	29.6	28.9	27.9	27.2	26.4	25.9	25.3	28.8
11000	38.0	36.4	35.0	33.5	32.4	31.5	30.4	29.4	28.7	27.9	27.2	26.6	25.9	30.1
11500	38.6	37.1	35.6	34.3	33.2	32.0	31.1	30.2	29.4	28.5	27.9	27.2	26.6	31.5
12000	39.4	37.7	36.2	35.0	33.7	32.8	31.7	30.9	30.0	29.2	28.5	27.7	27.2	32.9
12500	39.9	38.2	36.7	35.6	34.3	33.4	32.4	31.5	30.7	30.2	29.2	28.5	27.9	34.2
13000	40.5	38.8	37.5	36.2	35.0	33.9	33.0	32.0	31.3	30.6	29.8	29.0	28.5	35.6
13500	40.9	39.4	37.9	36.7	35.6	34.7	33.5	32.6	31.9	31.1	30.3	29.6	29.1	37.0
14000	41.4	39.9	38.4	37.3	36.2	35.0	34.1	33.2	32.4	31.7	30.9	30.2	29.6	38.4
14500	42.0	40.5	38.8	37.9	36.5	35.6	34.7	33.7	33.0	32.2	31.5	30.7	30.2	39.7
15000	42.4	40.9	39.5	38.4	37.1	36.2	35.2	34.3	33.5	32.8	32.1	31.3	30.6	41.1
15500	42.7	41.2	39.9	38.8	37.7	36.5	35.6	34.9	33.9	33.2	32.4	31.7	31.1	42.5
16000	43.1	41.8	40.5	39.2	38.0	37.1	36.2	35.2	34.2	33.5	32.7	32.2	31.5	43.8
16500	43.7	42.2	40.9	39.5	38.4	37.5	36.5	35.6	34.7	34.0	33.2	32.6	32.1	45.2
17000	44.0	42.5	41.2	40.1	39.0	37.9	37.1	36.2	35.2	34.4	33.7	33.2	32.6	46.6
17500	44.2	42.9	41.6	40.5	39.4	38.4	37.5	36.5	35.6	34.8	34.1	33.7	33.0	47.9
18000	44.6	43.3	42.0	40.9	39.7	38.8	37.9	36.9	36.0	35.3	34.5	34.1	33.4	49.3
18500	45.0	43.7	42.4	41.2	40.1	39.2	38.2	37.5	36.4	35.7	34.9	34.5	33.7	50.7
19000	45.4	43.9	42.7	41.6	40.5	39.5	38.6	37.9	36.8	36.0	35.3	34.9	34.3	52.0
19500	45.5	44.2	42.9	41.9	40.9	39.9	39.0	38.2	37.2	36.4	35.7	35.2	34.7	53.4
20000	45.9	44.6	43.3	42.2	41.2	40.1	39.4	38.6	37.5	36.8	36.1	35.6	35.0	54.8
20500	46.3	44.8	43.7	42.5	41.6	40.5	39.7	38.8	37.9	37.2	36.5	36.0	35.4	56.2
21000	46.5	45.2	44.0	42.9	41.8	40.9	40.1	39.2	38.2	37.5	36.8	36.4	35.8	57.5
21500	46.7	45.5	44.2	43.1	42.2	41.2	40.5	38.5	38.6	37.9	37.2	36.7	36.2	58.9
22000	47.0	45.7	44.6	43.5	42.5	41.6	40.7	39.9	38.9	38.2	37.5	37.1	36.5	60.3
22500	47.2	45.9	44.8	43.9	42.7	41.8	41.0	40.1	39.2	38.5	37.8	37.5	36.7	61.6
23000	47.4	46.3	45.0	44.0	43.1	42.8	41.2	40.5	39.5	38.8	38.1	37.7	37.1	63.0
23500	47.8	46.5	45.4	44.2	43.3	42.4	41.6	40.9	39.8	39.1	38.4	38.0	37.5	64.4
24000	48.0	46.7	45.6	44.6	43.7	42.7	41.8	41.0	40.1	39.4	38.7	38.2	37.9	65.8
24500	48.2	47.0	45.7	44.8	43.9	42.9	42.2	41.4	40.4	39.7	39.0	38.6	38.0	67.1
25000	48.4	47.2	46.1	45.0	44.0	43.3	42.4	41.6	40.7	40.0	39.3	38.8	38.2	68.5
25500	48.5	47.4	46.3	45.4	44.2	43.5	42.7	41.8	40.9	40.3	39.6	39.2	38.6	69.9
26000	48.7	47.6	46.5	45.5	44.6	43.7	42.9	42.2	41.2	40.5	39.8	39.5	38.8	71.2
26500	48.9	47.8	46.7	45.7	44.8	44.0	43.1	42.4	41.4	40.8	40.1	39.7	39.2	72.6
27000	49.1	48.0	46.9	45.9	45.0	44.2	43.3	42.7	41.7	41.0	40.4	39.9	39.5	74.0
27500	49.3	48.2	47.0	46.3	45.4	44.4	43.7	42.9	41.9	41.3	40.6	40.1	39.7	75.3
28000	49.5	48.4	47.4	46.5	45.5	44.6	43.9	43.1	42.2	41.5	40.9	40.3	40.0	76.7
28500	49.7	48.5	47.6	46.7	45.7	44.8	44.0	43.3	42.4	41.8	41.1	40.5	40.2	78.1
29000	49.9	48.7	47.8	46.7	45.9	45.0	44.2	43.7	42.9	42.2	41.6	41.0	40.5	79.4
29500	50.0	48.9	48.0	47.0	46.1	45.4	44.6	43.9	43.1	42.4	41.8	41.2	40.7	80.8
30000	50.2	49.0	48.2	47.2	46.3	45.5	44.8	44.0	43.3	42.7	42.0	41.4	40.9	82.2

Table 22.2. *Continued*

4% milk, pounds per year. (*FCM*)	Body Weight, Pounds													4% milk, pounds per day
	600	700	800	900	1000	1100	1200	1300	1400	1500	1600	1700	1800	
30500	50.2	49.1	48.3	47.4	46.5	45.7	45.0	44.2	43.7	42.9	42.4	41.6	41.1	83.6
31000	50.4	49.3	48.4	47.6	46.7	45.8	45.2	44.4	43.8	43.1	42.5	42.0	41.4	84.9
31500	50.6	49.5	48.5	47.7	46.9	46.1	45.4	44.6	43.9	43.3	42.7	42.2	41.6	86.3
32000	50.7	49.7	48.7	47.8	47.0	46.3	45.5	44.8	44.0	43.5	42.9	42.4	41.8	87.7
32500	50.8	49.9	48.9	48.0	47.2	46.5	45.7	45.0	44.2	43.7	43.1	42.5	42.0	89.0
33000	51.0	50.0	49.0	48.2	47.4	46.6	45.9	45.2	44.6	43.9	43.3	42.7	42.2	90.4
33500	51.1	50.1	49.1	48.3	47.5	46.7	46.1	45.4	44.7	44.0	43.5	42.9	42.4	91.8
34000	51.2	50.2	49.3	48.4	47.6	46.8	46.3	45.5	44.8	44.2	43.7	43.1	42.5	93.2
34500	51.4	50.4	49.4	48.5	47.8	47.0	46.4	45.7	45.0	44.4	43.9	43.3	42.7	94.5
35000	51.5	50.5	49.5	48.7	48.0	47.2	46.5	45.9	45.3	44.6	44.0	43.5	42.9	95.9
35500	51.5	50.6	49.7	48.9	48.2	47.4	46.7	46.1	45.4	44.8	44.2	43.7	43.1	97.3
36000	51.7	50.8	49.9	49.0	48.3	47.6	46.9	46.2	45.5	45.0	44.4	43.9	43.3	98.6
36500	51.9	50.9	50.0	49.1	48.4	47.7	47.0	46.3	45.7	45.2	44.6	44.0	43.5	100.0
37000	51.9	51.0	50.1	49.3	48.5	47.8	47.2	46.5	45.9	45.4	44.7	44.2	43.7	101.4
37500	52.0	51.2	50.2	49.5	48.6	47.9	47.3	46.7	46.0	45.5	44.8	44.3	43.8	102.7
38000	52.1	51.3	50.4	49.6	48.7	48.0	47.4	46.9	46.1	45.6	45.0	44.4	43.9	104.1
38500	52.3	51.4	50.5	49.7	48.9	48.2	47.5	47.0	46.3	45.7	45.2	44.6	44.0	105.5
39000	52.3	51.4	50.6	49.8	49.1	48.4	47.6	47.1	46.5	45.9	45.3	44.8	44.2	106.8
39500	52.5	51.5	50.8	49.9	49.2	48.5	47.8	47.2	46.6	46.0	45.4	45.0	44.4	108.2
40000	52.5	51.5	51.0	50.0	49.3	48.7	48.0	47.4	46.7	46.1	45.5	45.2	44.6	109.6

meaning that 0.305 lbs *TDN* is used for producing 1 lb *FCM*, not counting maintenance, and 0.053 lb *TDN* per unit $W^{0.73}$ is used for maintenance.

Now we defined dairy merit by the relation

$$\text{Dairy merit} = 100\,\frac{340 \times FCM}{1814 \times TDN} \tag{2}$$

The *TDN* is used for two purposes, (1) for producing *FCM* at the rate of 0.305 lb *TDN* for 1 lb *FCM* and (2) for maintenance at the rate of 0.053 lb *TDN* for one unit $W^{0.73}$. Therefore, equation (2) becomes, on substituting the values from equation (1),

$$\begin{aligned}\text{Dairy merit} &= 100\,\frac{340FCM}{1814(0.305FCM + 0.053W^{0.73})}\\ &= 100\,\frac{340FCM}{553FCM + 96.1W^{0.73}}\\ &= \frac{61FCM}{FCM + 0.173W^{0.73}}\end{aligned} \tag{3}$$

The factor 61, of course, represents the percentage of *TDN* energy converted to *FCM* energy above the maintenance level, not counting the maintenance cost. It means that the *net* energetic efficiency of milk production (not including the maintenance cost) is 61 per cent.

The dairy merit may thus be estimated from equation (3) or more conveniently from Table 22.2 or Fig. 22.2 even though the *TDN* consumption is not known. The *FCM* production and the body weight are the only data needed.

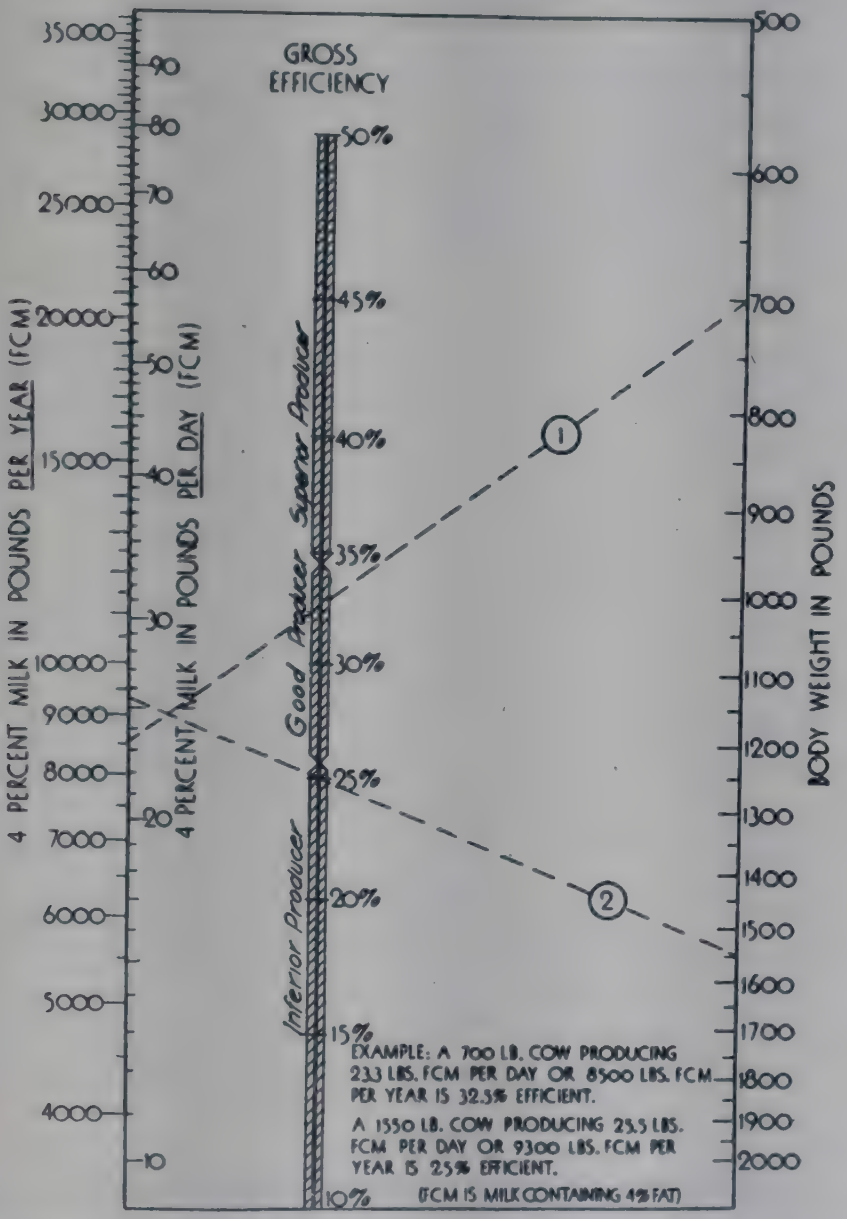

Fig. 22.2. This alignment chart may be employed for estimating gross efficiency of the milk production *process*, that is, the dairy merit of the *cow*. First, the pounds of the given milk are converted to pounds "FCM", that is, to milk containing 4 per cent fat (Table 22.3). The efficiency of milk production is then read from this chart. Thus if it is desired to find the dairy merit, or gross energetic efficiency, of a 700-pound cow producing 8500 pounds yearly or on the average 23.3 pounds daily of FCM (4 per cent milk), place a straight edge between 23.3 on the left (or milk) scale, and 700 on the right (or body-weight) scale, and read the answer 32.5 on the center (or efficiency) scale.

By way of further elucidation of Table 22.2 the following figures indicate how *FCM* production increases with body weight, assuming that the dairy merit is 30 per cent, *i.e.*, that 30 per cent of the consumed *TDN* energy is converted into milk energy. The values are extrapolated low enough to include dogs, rabbits, rats, and so on.

FCM Production in Relation to Body Weight When 30% of *TDN* Energy Is Converted to Milk Energy

Body weight (lbs)	*FCM* production (lbs/day)	Body weight (lbs)	*FCM* production (lbs/day)	Body weight (lbs)	*FCM* production (lbs/day)	Body weight (lbs)	*FCM* production (lbs/day)
1800	39.5	1100	27.5	400	13.0	10.0	0.88
1700	38.0	1000	26.0	300	10.5	5.0	0.53
1600	36.0	900	24.0	200	7.8	1.0	0.16
1500	34.0	800	21.0	150	6.4	0.7	0.126
1400	33.0	700	19.6	100	4.7	0.1	0.030
1300	31.5	600	17.5	75	3.8		
1200	29.0	500	15.3	50	2.9		

Summarizing, it is suggested that the dairy value of cattle be estimated not by the absolute amounts of milk production, because this varies with body weight, nor by the ratio of milk production to body weight (unless the range in weight is narrow), because this ratio necessarily declines with increasing body weight, but by the ratio $FCM/W^{0.7}$ or, preferably, by the dairy merit Table 22.2 or Fig. 22.2, defined as the percentage of *TDN* energy consumed, that is, converted into milk. *Dairy merit* in the *animal* is identical with *gross energetic efficiency* of the milk production *process*.

22.4: The influence of dairy merit on profit in animals of equal body weight. It is evident that, as the production level increases, the maintenance tax—including feed and labor—per unit milk production decreases. The labor per unit milk production decreases because it does not take much more time to milk, clean, feed, and manage a superior than a mediocre cow. In brief, the more milk a cow of a given weight produces, the greater the profit per head, per herd, and per pound of milk produced.

Roughly speaking, the total milk-production cost is double the feed cost for both high- and low-milking cows. This is exemplified by the following values.[9]

Influence of Milk Yield on Cost of Milk Production

Milk fat production (lbs/yr)	150	200	250	300	350	400	450
4%-milk production (lbs/yr)	3750	5000	6250	7500	8900	10000	11250
Estimated feed cost ($)	52	61	68	74	81	88	94
Estimated total cost ($)	104	122	136	148	162	176	188
Cost per 100 lbs of 4%-milk	2.77	2.44	2.18	1.97	1.85	1.76	1.67

As the milk yield increases, the feed cost *per unit milk* becomes less, because of the saving in the feed cost of maintenance per unit milk production. The decrease in *feed cost per unit milk* is paralleled by decrease in *labor cost per unit*

[9] Reported in chart form in the *American Dairyman* (Aug. 5, 1941). The values (except for the 4% milk row computed by the writer) were read from the chart by permission of Leland W. Lamb, who obtained the feed figures from the Dairy Records office, Cornell University. The body weights are not given and the significance of these values is, therefore, somewhat mixed. The increase in milk production is probably due in part to increased dairy merit, in part to increased weight, and in part to better feeding.

milk because it does not take more time to milk, feed, clean, etc. a superior than an inferior animal. It is concluded that profits per animal and per unit milk increase with increasing milk production in the approximate manner given in the above table.

22.5: The influence of body weight on profit in animals of equal dairy merit. The cost of milk production is usually divided into feed 50 per cent, and overhead 50 per cent (labor and management 30 per cent, miscellaneous 20 per cent). Since the overhead costs are substantial, it is necessary to discuss the influence of body weight upon them.

Table 22.3. Table for Converting Milk of Given Fat Percentage to "4 Per Cent Milk" by Means of Table 22.1*

A Per cent Fat in Milk	B Factor for Converting to 4% Milk	A Per cent Fat in Milk	B Factor for Converting to 4% Milk
2.5	0.775	5.0	1.150
2.6	0.790	5.1	1.165
2.7	0.805	5.2	1.180
2.8	0.820	5.3	1.195
2.9	0.835	5.4	1.210
3.0	0.850	5.5	1.225
3.1	0.865	5.6	1.240
3.2	0.880	5.7	1.255
3.3	0.895	5.8	1.270
3.4	0.910	5.9	1.285
3.5	0.925	6.0	1.300
3.6	0.940	6.1	1.315
3.7	0.955	6.2	1.330
3.8	0.970	6.3	1.345
3.9	0.985	6.4	1.360
4.0	1.000	6.5	1.375
4.1	1.015	6.6	1.390
4.2	1.030	6.7	1.405
4.3	1.045	6.8	1.420
4.4	1.060	6.9	1.435
4.5	1.075	7.0	1.450
4.6	1.090	7.1	1.465
4.7	1.105	7.2	1.480
4.8	1.120	7.3	1.495
4.9	1.135	7.4	1.510

Column A gives fat percentages, column B corresponding conversion factors, which when multiplied by pounds of milk produced, will convert the given milk to 4% milk. Thus if a cow produces 10,000 pounds of 3% milk multiply 10,000 by 0.850 and get the answer 8500 pounds of 4% milk. In other words 10,000 pounds of 3% milk contains the same amount of energy as 8500 pounds of 4% milk.

* The conversion factors in this table were computed from Gaines' formula "$FCM = .4M + 15F$, where FCM (fat-corrected milk) is gross energy value in terms of normal average cows' milk of 4 per cent fat content, M is actual milk and F is fat, all in the same unit of weight." (W. L. Gaines, Univ. Ill. Agr. Exp. Sta. Bull. 308, 1928.)

If *dairy merit is equal in large and small animals*, the larger the animal the more milk she will produce. Since it does not take more time to milk, feed, clean, and manage a large cow producing more milk than a small cow producing less milk, it is obvious that the labor and management and other overhead costs should be less for large than for small animals producing a given amount of milk.

By way of illustration, let us assume that it is desired to produce the equivalent of 1000 lbs of 4 per cent-milk (*FCM*) a day at a gross energetic efficiency of 30 per cent. It may be shown from the definition of gross energetic efficiency that 625 lbs *TDN* would be consumed per day to produce 1000 lbs milk (*FCM*) per day, *regardless of the size of animals.* The number of animals of different body weight required to produce the 1000 lbs (*FCM*) per day is given in the following table.

Influence of Body Size on Number of Animals Required to Produce 1000 lbs *FCM*/day at 30 per cent Efficiency

Weight of animal (lbs)	Number of animals required to produce milk at 30% efficiency
1700	26
1400	30
1000	38
900	42
700	53
100	200

Obviously it takes more labor to milk, feed, etc. 200 goats than 53 cows; 53 than 38 cows; 38 than 26 cows. Therefore, *per 1000-lbs* milk yield and when dairy merits are equal, the larger the animals, the fewer required to produce the milk, and the less the overhead costs per unit milk produced.

Using different wording, about twice as much milk (at nearly half the labor cost) may be produced from *a given number* of 1700-lb cows than from 700-lb cows, provided that the dairy merits of the two are equal; and a given number of large animals constitute a larger business with larger profits than small animals of the same dairy merit.

The following example illustrates how a difference in body size of an order frequently found in dairy herds, in animals of the *same dairy merit*, affects the monetary profit.

Assume that each of 2 groups of cow's produces 1000 lbs 4 per cent milk a day, selling at $2.00 per 100 lbs. The feed cost is the same, $1.50 per 100 lbs *TDN*; dairy merit of the cows, or the efficiency of milk production, is the same: 30 per cent of the *TDN* is converted into milk. The only difference is that in one group the animals weighed 900 lbs, in the other 1400 lbs. How do the two herds compare from the profit viewpoint? Solution:

	900-lb cows	1400-lb cows
No. cows needed to produce 1000 lbs. 4%-milk daily at 30% efficiency..........................	42	30
TDN needed to produce 1000 lbs. 4%-milk daily at 30% efficiency....................................	625 lbs/day	625 lbs/day
Milking time.	13.6 hrs	10 hrs
Housing, records, taxes, etc.........................	42x	30x

(x = 10¢ per cow per day)

Cost for 900-lb herd =	feed	$9.37
	labor	2.72
	records, etc.	4.20
		16.29

Cost for 1400-lb herd =	feed	$9.37
	labor	2.00
	records, etc.	3.00
		14.37

Return from milk = \$20 per day

Profit for the herd of 900-lb cows \$20.00 − \$16.29 = \$3.71 per day

Profit for the herd of 1400-lb cows \$20.00 − \$14.37 = \$5.63 per day

Relative profit $= \frac{5.63}{3.71} = 1.5$ as much for the herd of 1400-lb cows as for the 900-lb cows.[8a]

The above computations indicate that if dairy merit and price per unit 4 per cent-milk are the same for milk of the small and large cows, the profit on a *given amount of 4 per cent-milk* produced is 50 per cent greater when produced by the 1400-lb than by the 900-lb cows. The profit differences, of course, increase with increasing body-size differences. This type of reasoning is not applicable with the same force to pasture fed cattle where the housing and management items are of a different order.

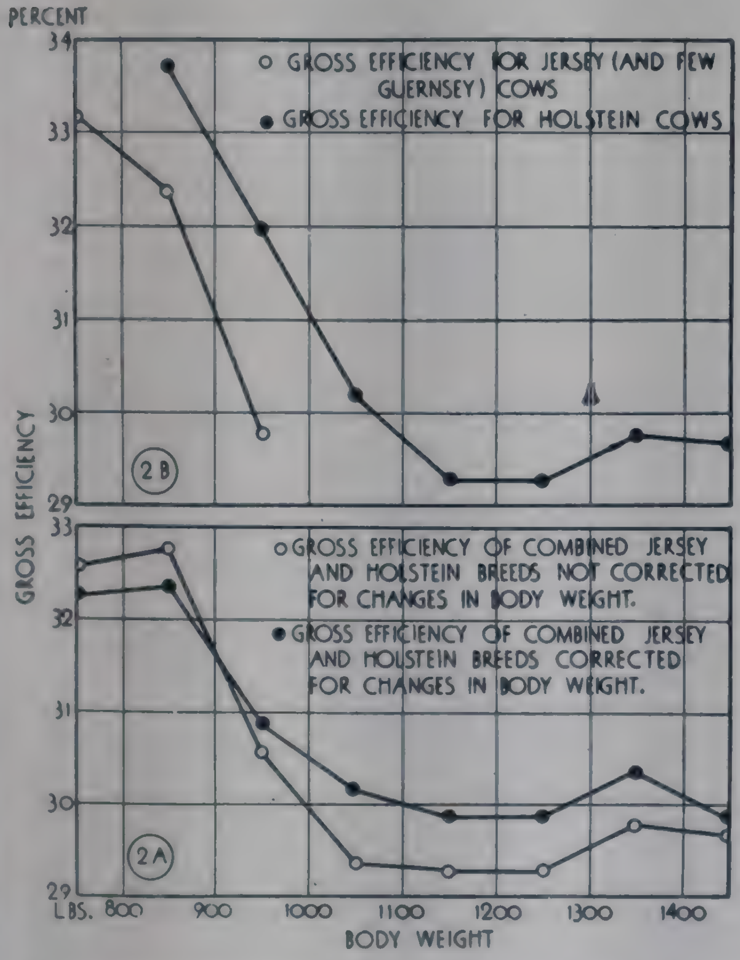

Fig. 22.3a.
The gross efficiency of milk production tends to decline with increasing body weight.

The above estimates are based on the assumption that dairy merit and other conditions are equal in large and small cows, which may not be the case. Small cows tend to be more efficient than large ones (Fig. 22.3) because the basis for selection has been the production *per cow*. To stay in the herd the small cow has had to produce nearly as much milk as the big cow; but if the small cow produces as much as the big one, she is more efficient because she has a smaller body to maintain, and so she expends less of her feed for maintenance.

[8a] Since the above was written, a release from Cornell University (reported in *The Surge News*, Aug. 1944) indicates that the "labor income" from milk production on one fourth of 558 dairy farms with the highest average weight per cow (1140-lb cows producing 7886 lbs of 3.7 per cent milk) was \$944 as contrasted to \$207 "labor income" on one fourth of the farms with the lowest average weight per cow (792-lb cows producing 5070 lb of 3.7 per cent milk). An increase of 100 lbs in live weight was associated with a 500 to 800 lbs increase in yearly milk yield.

The fact that large animals are, on the average, less efficient than small ones presents the greater opportunity for raising the efficiency of the large cows, and Table 22.2, or Fig. 22.2, furnishes the necessary (tentative) yardstick for measuring dairy merit of cows, regardless of their body size.

Many practical considerations confuse the size factor. For instance some milks are especially in demand for fluid consumption; others for butter production; still others for cheese production. Table 22.4 shows why some milks are preferred for butter and others for cheese—some are relatively richer in fat, others in casein. Color is also a factor.

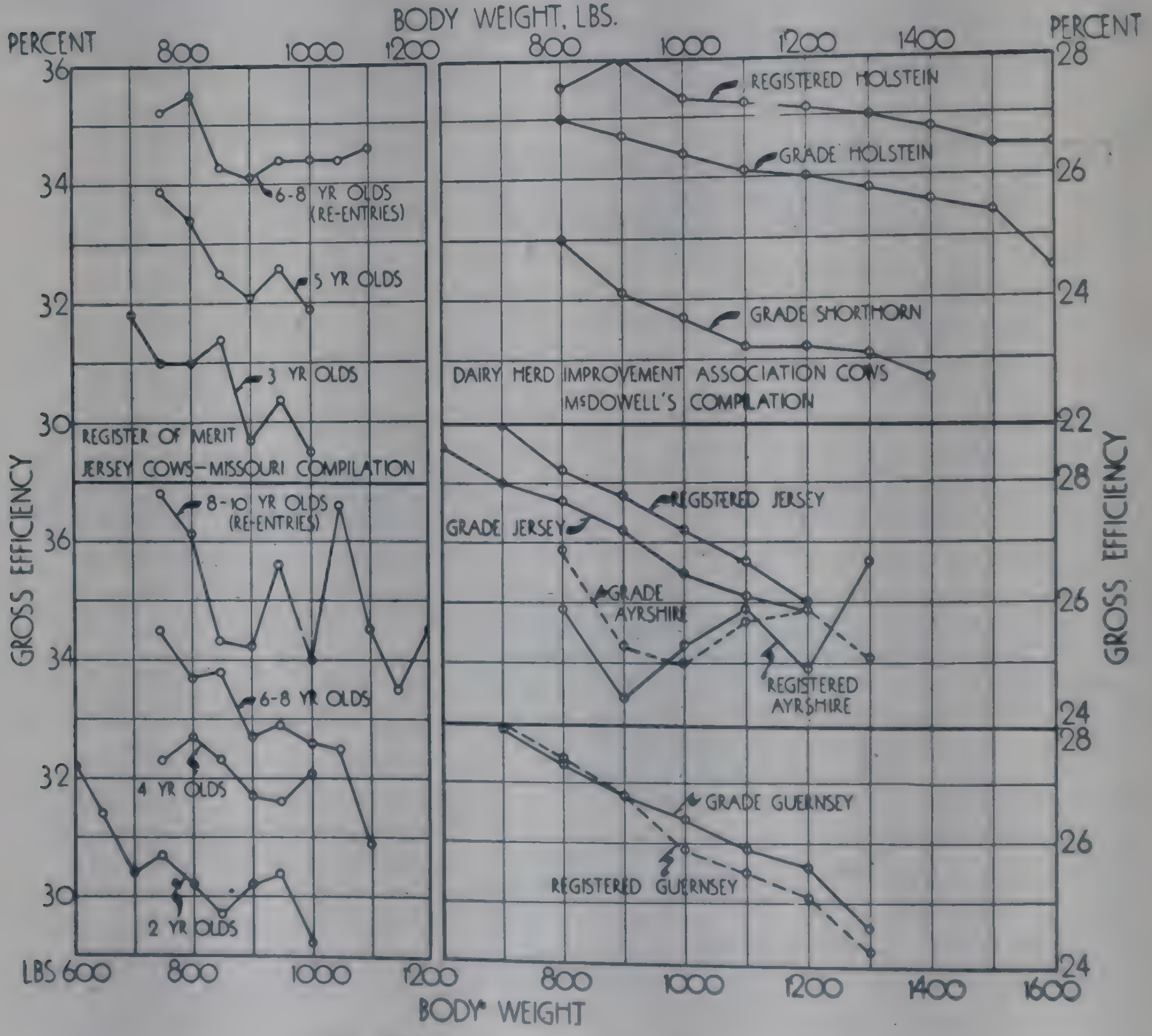

Fig. 22.3b. See legend for Fig. 22.3a.

Topography and climate may favor one or another size of cow. Thus large cows have greater difficulty in grazing on steeply-rolling pastures than small ones, especially on poor pastures which involve much movement. Large animals have a smaller surface area (for dissipating heat) per unit weight than small animals (Ch. 13), and in hot weather large animals may, perhaps, not be able to keep as comfortably cool as small ones (however, the extent of

Table 22.4. The Relation Between the Percentages of Fat, Protein and Lactose[1]

	Protein, %						Lactose, %						Ratio fat to protein						Ratio fat to lactose						Ratio protein to lactose					
Fat, %	Ayrshire	Brown-Swiss	Holstein	Guernsey	Jersey	Goats	Ayrshire	Brown-Swiss	Holstein	Guernsey	Jersey	Goats	Ayrshire	Brown-Swiss	Holstein	Guernsey	Jersey	Goats	Ayrshire	Brown-Swiss	Holstein	Guernsey	Jersey	Goats	Ayrshire	Brown-Swiss	Holstein	Guernsey	Jersey	Goats
3.0	3.1	3.3	3.0			2.9	4.6	5.1	4.9			4.3	.97	.90	.98			1.0	.66	.58	.61			.69	.68	.65	.62			.67
3.5	3.3	3.4	3.4		3.4	3.1	4.6	5.1	4.9			4.4	1.0	1.0	1.0		1.0	1.1	.76	.69	.72			.80	.72	.67	.70			69
4.0	3.5	3.6	3.7	3.5	3.5	3.2	4.7	5.1	4.8	4.9	5.0	4.5	1.1	1.1	1.1	1.2	1.2	1.2	.85	.79	.83	.81	.80	.89	.74	.71	.77	.71	.69	.72
4.5	3.7	3.7	4.1	3.7	3.6	3.4	4.7	5.0	4.8	4.9	5.0	4.5	1.2	1.2	1.1	1.2	1.2	1.3	.95	.90	.94	.91	.90	.99	.78	.73	.85	.74	.72	.74
5.0	3.9	4.1	4.4	3.9	3.8	3.5	4.8	5.0	4.7	4.9	5.0	4.6	1.3	1.2	1.1	1.3	1.3	1.4	1.0	1.0	1.0	1.0	1.0	1.1	.81	.82	.93	.80	.76	77
5.5	4.1	4.4	4.7	4.2	4.0	3.7	4.8	4.9	4.7	4.9	5.0	4.7	1.3	1.2	1.2	1.3	1.4	1.5	1.1	1.1	1.2	1.1	1.1	1.2	.84	.90	1.0	.84	.80	79
6.0		4.9	5.1	4.4	4.1	3.8		4.9	4.7	4.9	5.0	4.8	1.2	1.2		1.4	1.5	1.6		1.2	1.3	1.2	1.2	1.3		1.0	1.1	.90	.83	.81
6.5		5.4		4.6	4.2					4.8	4.9			1.2		1.4	1.6					1.3	1.3					.95	.86	
7.0				4.8	4.3					4.7	4.9					1.5	1.7					1.5	1.4					1.0		

McDowell[2]

Influence of fat percentage in milk on cheese production

Fat %	Casein %	Casein to fat ratio	Cheese/lb. fat, lbs.	Cheese/100 lbs. milk, lbs.	Fat in whey, % (Cheddar cheese)
3.0	2.3	0.75	2.8	8.5	0.3
3.5	2.4	0.70	2.6	9.5	0.25
4.0	2.6	0.65	2.5	10.2	0.38
4.5	2.7	0.60	2.4	10.9	0.34
5.0	2.8	0.55	2.3	11.7	0.35
5.5	2.9	0.52	2.4	12.5	0.46
6.0	3.1	0.50	2.4	13.2	

Eckles and Shaw[3]

Month Lactation	Fat	Casein %	Casein to fat ratio
1	4.0	2.7	.67
2	3.9	2.4	.61
3–7	3.8	2.5	.69
8	3.9	2.7	.71
9	4.0	2.9	.72
10	4.1	3.1	.75
11	4.2	3.2	.76
12	4.5	3.4	.75
13	4.7	3.6	.78

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[1] From smoothed curves of data obtained from many sources especially from H. C. Lythgoe "Composition of goat milk of known purity" *J. Dairy Sci.*, **23**, 1097 (1940) and Overman, O. R., Garrett, O. F., Wright, K. E., and Sanmann, F. P., "Composition of milk of Brown Swiss cows." Univ. Ill. Agr. Exp. Sta. Bull. 457, 1939.

[2] McDowell, F. H.; *J. New Zealand J. Sci. Tech.*, **18**, 137 (1936).

[3] Eckles, C. H., and Shaw, R. H., U.S. Bureau Animal Industry, Bulls. 155, 156, 157, 1913.

surface area per unit weight is only one of many factors involved in keeping cool, see Ch. 11).

There are other factors, no doubt, such as the clumsiness of larger cows (Ch. 17) and their greater probability to injury, leg and hoof troubles, and so on, which may counteract the obviously desirable features of large animals. However, when *all conditions are equally favorable for both*, large cows are more profitable for large-scale milk production; in a barn with a given number of stanchions one can produce more milk with large cows than with small ones of the same dairy merit and reduce the production cost per unit milk proportionately.

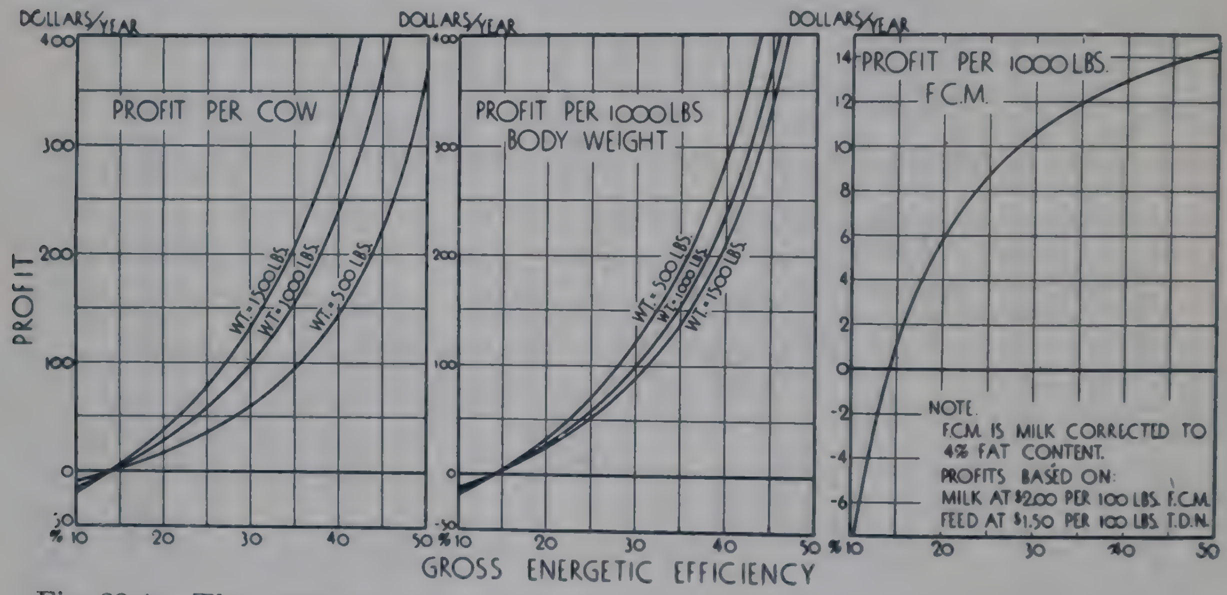

Fig. 22.4a. The profit of income from milk over cost of feed as function of dairy merit of the cow (gross energetic efficiency of milk production). The two left curves would be much steeper if the other expenses (labor, etc.) were included in the cost, and the curve on the right would bend upwards instead of downwards. Note that profit rises more steeply than energetic efficiency; while profit rises directly with the FCM yield, energetic efficiency increases at decreasing increments. Note also that at 30 per cent efficiency the income from milk is $70 above the feed cost for the 500-lb. cow; $100 for the 1000-lb. cow; $130 for the 1500-lb. cow.

In summary, we should like to modify the phrase used by McDowell[10] "within the breed big dairy cows excell," to "within a dairy-merit class big dairy cows excell." McDowell was only partly right in his conclusion. Large cows may or may not excell within or without the breed, depending on the relative dairy merits of the large and small cows.

22.6. The influence of the plane of nutrition on profit. The plane of nutrition of a given animal is defined by comparison with some feeding standard as reference base, for instance Haecker's feeding standard taken as 100 per cent.

The influence of the plane of gross (feed) energy intake on net (milk energy, meat energy, etc.) energy production was discussed in Chapter 5, as one example of the principle of diminishing increments (Fig. 5.1). This principle was there illustrated profusely in relation to milk production by tables and charts which may be summarized as follows.

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[10] McDowell, J. C., *U. S. Dept. Agr. Circ.*, 114, 1930.

The greater the feed consumption the greater is the milk production, but the *milk production per unit grain* or *per unit TDN consumption*, or the *percentage of TDN Calories converted into milk Calories* (apparent dairy merit) declines with increasing plane of nutrition.

Since, however, the production per cow is increased, the profit per cow, per stanchion, and therefore for the whole herd tends to increase, as shown by Borland's data (Ch. 5). (See also Fig. 22.4a.) The profit per cow in Borland's table refers to that of milk income over feed expenditures (not counting the other 50 per cent of the expenses, for labor, etc.). The profit would increase more rapidly with increasing plane of nutrition if the other expenses were included, especially labor, since the labor cost of feeding, milking, cleaning, etc., is no greater for milking the larger than the smaller amounts of milk.

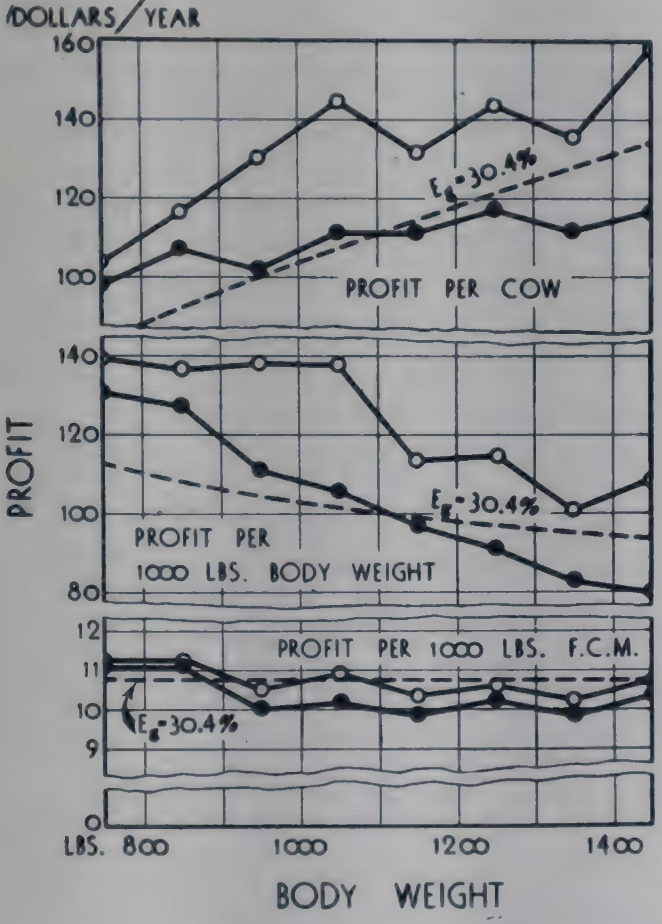

Fig. 22.4b. Influence of live weight on profit per cow (top segment), per 1000 pounds body weight (middle segment), and per 1000 pounds milk (FCM) production (bottom segment). The light broken curves indicate the effect when gross energetic efficiency is assumed to be the same, namely, 30.4 per cent for all live weights. The continuous curves represent the observed data. Profit is defined by the difference between monetary return for milk at $2.00 per 100 pounds FCM and monetary cost of feed at $1.50 per 100 pounds TDN, ignoring all other expenses. While the profit *per unit milk* is the same in small and large cows, the profit per cow, per stanchion, and therefore for the herd increases very rapidly with increasing live weight, at the *same dairy merit* of 30.4 per cent.

Profit, of course, also depends on the relative prices of milk and feed (Table 22.5).

The high feeding level may, sometimes, have unfavorable long-range effects, such as development of mastitis, milk fever, and so on. The actual situation is more complex than can be indicated by a table or graph.

Summarizing, average dairy animals produce about 80 per cent as much milk energy on an exclusive, good, roughage ration as they do on such a ration supplemented with about 1 lb grain per 6 lbs milk (*FCM*), as called for by the Haecker Standard. On the other hand, milk production may be increased by about 20 per cent above the level attained by the Haecker Standard by additional grain. The amount of increase depends on the dairy merit of the animal, on her capacity to utilize the extra nutrients (Ch. 5). The increased *TDN* consumption, brought about by increased grain allowance, tends to increase the milk yield at decreasing increments with successive feed units in accordance with the principle of diminishing increments, but often with increasing monetary returns.

22.7: Summary. Each of the three components (1) dairy merit, (2) body size, and (3) plane of nutrition involved in the lactational level, and therefore in the profit complex, is defined and analyzed while holding the other factors constant. These analyses may be briefly summarized as follows.

Table 22.5. Suggested grain-feeding schedules for different price relations, based on a daily roughage portion of 20 pounds of ordinary hay per 1,000-pound cow*

Section A Pounds daily production of milk, testing—				Section B Pounds grain to feed for greatest profit when grain price is—				
3½ per cent fat	4 per cent fat	4½ per cent fat	5 per cent fat	1½ times milk price or .07 times fat price	1¼ times milk price or .06 times fat price	Same price as milk or .05 times fat price	¾ of milk price or .04 times fat price	½ of milk price or .03 times fat price
11	10	9	8	2	2	2	3	4
17	15	14	12	4	4	5	6	7
22	20	18	16	6	6	7	8	10
28	25	23	21	8	8	9	11	13
33	30	27	25	10	11	12	13	16
39	35	32	29	12	13	14	16	19
45	40	36	33	14	15	16	19	22
50	45	41	37	16	17	19	21	25
56	50	45	41	18	19	21	24	
61	55	50	45	20	21	23	Commercial dairymen seldom feed more than 25 pounds	
67	60	54	49	21	23			

* Courtesy U. S. D. Agr., Bureau of Dairy Industry.

(1) *Dairy merit* is defined by the percentage of the consumed *TDN* energy that is converted into milk energy.

The dairy merit of "good" dairy cows is approximately 25 per cent; one-fourth of the consumed *TDN* energy is converted into milk energy. This 25 per cent dairy-merit level pays, approximately, for the dairyman's work, feed, and other expenses at the current rate. "Making money" on cows involves higher dairy merit. What are usually called "superior cows" have a dairy merit of about 33%. The following table indicates in round numbers the milk (*FCM*) production for cows of different weight at dairy-merit levels of 25 and 33 per cent.

Milk Production, lbs *FCM*, for Cows of 25 and 33 per cent Dairy Merit

Body weight (lbs)	25% efficiency		33% efficiency	
	FCM/yr	*FCM*/day	*FCM*/yr	*FCM*/day
600	4700	13	7700	21
700	5100	14	8700	24
800	5800	16	9500	26
900	6200	17	10600	29
1000	6900	19	11600	32
1100	7300	20	12400	34
1200	7700	21	13100	36
1300	8000	22	13800	38
1400	8700	24	14600	40
1500	9100	25	15300	42
1600	9500	26	16000	44
1700	9800	27	16800	46
1800	10200	28	17500	48

Dairy merit is apparently independent of body weight *as such.* Rats, dairy goats, and dairy cattle of all sizes may convert up to about 50 per cent of the ingested *TDN* energy into milk energy. Dairy cattle do not naturally belong to this high-lactation class; they were chosen *by man* because of the size, temperament, and grazing qualities; then by selection developed into high and prolonged milkers.

Small cows, especially within the breed, usually have a higher dairy merit than large ones. This is because of the tendency to evaluate performance by *absolute* milk production rather than by dairy merit, *i.e.*, by the *ratio* of milk produced to feed consumed; so that only such small cows survive in the herd as produce almost as much as the large ones. If a small animal produces as much as a larger one she is more efficient because the small one uses less feed for the maintenance of her smaller body.

It is indicated that the 1700-lb cow that produced the fabulous 1400 lbs butterfat in a year, equivalent to about 42,000 lbs 3.3 per cent-fat milk, has an appreciably lower dairy merit than the 700-lb cow that produced 26,000 lbs *FCM* in a year. Assuming that large cows are biologically capable of developing to the same dairy-merit level as small ones, we shall have 1700-lb cows producing the equivalent of about 50,000 lbs *FCM*, or 2000 lbs butterfat in a year, equivalent in terms of dairy merit to the 26,000 lbs *FCM*, or 1040 lbs butterfat in a year produced by the 700-lb cow.

From the viewpoint of dimensional analysis (Ch. 17), dairy merit may be thought of as the *intensity factor* in the lactational process.

(2) The *capacity factor* in the lactational process is body size—not simple weight, W, but *lactationally effective* body size, which appears to be best represented by $W^{0.7}$. This means that increasing body weight 100 per cent increases milk production by only about 70 per cent.

(3) A formula is presented $\left(\text{dairy merit ratio} = \frac{61FCM}{FCM + 0.173W^{0.73}}\right)$ and

a table based thereon, Table 22.2, from which the dairy merit ratio may be estimated if *FCM* and *W* (body weight) are known. It is suggested that this table be employed for estimating dairy merit. If Table 22.2 is sound, a yardstick is made available for measuring lactational ability or dairy merit *independently of body size*. Its usefulness in selecting superior dairy animals may, perhaps, turn out to be comparable in value to that of the Babcock fat test.

(4) It appears that a good roughage, without grain supplement, fed *ad libitum* to "good" dairy cows, yields about 20 per cent less milk than if the roughage is supplemented with about 1 lb grain per 6 lbs milk (*FCM*). Supplementing this Haecker-Standard ration by still more grain increases the milk production to about 20 per cent above the Haecker Standard-fed cows; but the yield increase occurs at decreasing increments in accordance with the principle of diminishing returns (Fig. 5.1). The grain allowance is governed by the quality of the cow, relative costs of feed, labor, and miscellaneous expenses on one hand and the price of milk on the other.

(5) It was shown by a numerical example, involving payment for labor, management, and housing, and when *all other conditions are equal*, that the profit on 1400-lb cows (30 of which are required to produce 1000 lb *FCM* at 30 per cent efficiency) is about 50 per cent greater than on 900-lb cows (42 of which are required to produce 1000 lbs *FCM* at 30 per cent efficiency). Needless to say, "all other conditions" are never equal. There are differences in market demand and in price; in topography and climate; in ability to graze on rolling country and to withstand heat and drought; in clumsiness of larger animals; in greater efficiency of smaller animals as a result, not of body size *as such*, but of the more intensive selection that has been practiced on the smaller animals, and so on, which may nullify, in part, the above generalization concerning the greater profitableness of large animals. This, then, is in the nature of a general rule, and like other general rules has many exceptions. The importance of the exceptions to this general rule will be reduced in proportion to the increase in equitable standardization of milk quality, standardization in feeding, management, and housing conditions, and standardization in selection and breeding on the basis of dairy merit (rather than on the basis of absolute milk yield, which is ambiguous because of its dependence on body size as well as on dairy merit).

Chapter 23

Egg Production: Nutritional and Energetic-Efficiency Aspects

> Whereas the nourishment milk is produced for mammals in the breasts, nature does this for birds in the egg. *Aristotle*

23.1: Similarities and differences between egg and milk. Most of the discussion in the preceding two chapters on milk production is applicable to egg production. Poultry, like dairy cattle, convert feed stuffs not suitable for human consumption into food highly prized in the human diet. While the monetary value of eggs produced is, in total, less than that of milk, more farms produce eggs than milk. Egg, like milk, is a secretory product of the reproductive system, and the physicochemical, metabolic, and endocrine mechanisms of egg production are similar to those of milk production.

The reliance of the avian embryo on egg nutriment is more absolute than of the mammalian infant on milk nutriment, because the infant at birth is already in possession of many nutrients stored in the liver and elsewhere. The egg must, therefore, be very perfectly adjusted for supporting rapid avian growth and development.

The closed-in, or cleidoic (Needham), arrangement of the egg imposes certain characteristics on its nutritional properties. Thus, the cleidoic arrangement demands that the egg nutriment be very concentrated; since per unit bulk, fat is more concentrated calorically than sugar, the egg fuel is in the form of fat rather than sugar.

Because every cell has a cholesterol framework, egg is rich in cholesterol, a substance not utilized advantageously in the less rapidly growing, or in adult, humans; and some older individuals may have difficulty in disposing of it.[1]

Like milk and meat, egg is an excellent vitamin-mineral-protein supplement to the prevailing high-calorie but vitamin-mineral poor bread-potato-sweets diet. While egg is more expensive per pound or per calorie than milk, it is richer in many supplementary nutrients as indicated in Table 23.1.[2] Thus per pound as purchased, egg contains twice as much energy, fat, P, and vitamin B_2 (riboflavin); three times as much protein; four times as much vitamin A; eight times as much vitamin B_1 (thiamine); and twelve times as much iron and copper (Tables 23.1b to c).

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[1] This is debatable. For a review of cholesterol in the diet, see Brody, S., *Ann. Rev. Biochem.*, **4**, 386–91 (1935).

[2] Berryman, G. H., and Chatfield, Charlotte, *J. Nut.*, **25**, 27 (1943).

Of course, milk is very much richer in edible calcium and sugar. Market egg contains practically no sugar, whereas milk contains nearly 5 per cent of the uniquely valuable lactose. Egg is very rich in calcium—about 2 gm calcium per egg as contrasted to 1.1 gm per quart milk—but most of it is in the shell. The edible part of the egg contains about one-third as much calcium as milk.

There are many ways of comparing nutritive values of foods, and Table 23.1 compares egg and milk in two other ways—per 100-gm and per 100-Calorie portions. The slight discrepancies between the three tables should not be disturbing considering the biological variability of the material. (All numbered tables are listed at the end of this chapter.)

The proximate composition values are from Chatfield and Adams;[3] minerals from Rose and Vahlteich;[4] vitamins from Daniel and Munsell,[5] Fixsen and Roscoe,[6] Sherman and Lanford;[7] the composition of 100-Calorie portions from Hawley and Maurer-Mast,[8] slightly modified.

The vitamin concentration of egg is sensitive to that in the feed. Thus[9] vitamin A was increased five-fold, D ten-fold, B_2 twice in eggs of chickens transferred from indoor to a blue-grass pasture in the sun. Feeding cod-liver oil increased the vitamins A and D in similar manner. The iodine content of egg was increased over 100-fold by dietary method.

The variations in protein and fat of eggs and their responses to the dietary supplies are perhaps of the same order as in milk.[10]

Stiebeling[11] estimates that about twenty cents of the consumer's dollar is spent for dairy products (which furnish approximately 20 per cent of the Calories in a good diet, 16 per cent of the protein, 62 per cent calcium, 30 per cent vitamin A, 35 per cent vitamin B_2, 5 per cent vitamin C) and about five cents for eggs (which furnish approximately 1.7 per cent of the dietary calories, 4.9 per cent of the protein, 2.7 per cent of the calcium, 6 per cent vitamin A, and 5 per cent vitamin B_2). Milk selling at 14 cents a quart furnishes *calories* at the same price (two cents per 100 Calories) as eggs selling at approximately 20 cents a dozen.[12] It is, however, unfair to compare milk and eggs on a cost-per-calorie basis, since eggs are not eaten for calories, which are best obtained from bread and potato.

In his encyclopedic "Chemical Embryology," Needham cites extensive data on the variability of eggs in weight and composition. For the present it is sufficient to say that the market egg of the domestic fowl weighs about two ounces (55-59 gm), of which about 11 per cent is shell, 30 per cent yolk, 59 per cent white. We found[13] the fuel value of the 58-gm egg to be of the order of 90 Cal. Computation from Chatfield and Adams' table yields 78 Cal. The average market egg on which Chatfield and Adams' averages are based probably weighs less than 58 gm.

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[3] Chatfield, C., and Adams, G., *U. S. Dept. Agr. Circ.*, 549, 1940.

[4] Rose, M. S., and Vahlteich, E. M., *J. Am. Diet. Assn.*, **14**, 593 (1938).

[5] Daniel, E. P., and Munsell, H. E., *U. S. Dept. Agr. Misc. Pub.*, 275, 1937.

[6] Fixsen, M., and Roscoe, H., *Nut. Abst. and Rev.* **7**, 823 (1938).

[7] Sherman, H. C., and Lanford, C. S., *J. A. M. A.*, **110**, 1278 (1938), also "Essentials of nutrition," Macmillan, 1940.

[8] Hawley, E. E., and Maurer-Mast, E. E., "The fundamentals of nutrition," Thomas, 1940.

[9] Bethke, R. M., *et al.*, *J. Biol. Chem.*, **72**, 695, 1927; *J. Nut.*, **12**, 309 (1936); *J. Poultry Sci.*, **15**, 326 and 336 (1936).

[10] Titus, H. W., Byerly, T. C., and Ellis, N. R., *J. Nut.*, **6**, 127 (1933); *J. Agr. Res.*, **53**, 453 (1936).

[11] Stiebeling, H. K., Bureau Labor Statistics, U. S. Dept. Labor Serial R409, 1936, and "Year Book of Agriculture," U. S. Dept. Agriculture, 1939.

[12] Let 1 qt milk = 700 Cal selling at 14 cents; and 1 doz eggs = 1000 Cal. Therefore a dozen eggs should sell to give the same price *per Calorie*, $14 \times \frac{1000}{700} = 20$ cents a dozen.

The yolk weighs about 17.4 gm, the white 34.2 gm, the shell 6.4 gm. The protein weighs about 7 gm, the fat 6.7 gm. The white weighs twice as much as the yolk, but the fuel value of the white is only one-fourth that of the yolk, because: (1) the yolk has 51 per cent solids as compared to the 12 per cent solids of white, and (2) the yolk solids are mostly fat (63 per cent fat, 33 per cent protein) as contrasted to white solids, practically all protein. (The watery nature of egg white suggests that its function is similar to that of the jelly of frog eggs: it is principally a water reservoir for the embryo).

The following notes outline the reasons for the longer time taken to produce unit egg energy than unit milk energy.

The germ cell (germinal disk when not fertilized, blastoderm when fertilized) and the surrounding nutrient yolk are wrapped in the vitelline membrane (Fig. 23.1a). The yolk is composed of a series of concentric dark and light layers. The dark yolk is in turn composed of structural units ranging in size from 0.025 to 0.100 mm in diameter, and the light yolk of units up to 0.07 mm.

The albumen is also made up of several layers. Closely adhering to the vitelline membrane is the dense chaliziferous layer connected with the chalazae. This layer is surrounded by the "dense white" layer which comprises 40 to 60 per cent of the total egg white. This layer is a fibrous meshwork filled with thin albumen. Surrounding this fibrous layer is a more liquid mucilagenous albumen layer. The yolk and albumen are packaged in a shell composed mostly of $CaCO_3$ (93–98 per cent) lined with outer and inner shell membranes.

Fig. 23.1b indicates the time relations *in the oviduct* as reported by Warren and Scott.[14] The germ and yolk are formed in the ovary; the albumen, shell membranes, and shell in the oviduct.

When the yolk is fully formed, the follicle housing it ruptures, and the germinal disk and yolk system escape into the infundibulum, or funnel, of the oviduct. Fertilization occurs in the infundibulum, and within about half hour of its arrival the egg departs for a journey of about 25 hours, travelling slowly through the magnum (about 3 hours), isthmus (about 1½ hours), uterus (about 20 hours), vagina (about ½ hour). Most of the albumen, including the chalazae, is secreted in a period of about 3 hours in the albumen-secreting portion of the oviduct, and the remaining in the isthmus and uterus sections. The membranes are formed in the isthmus, and the shell in the uterus.

But the time factor in the formation of albumen and shell in the oviduct is only one,

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[13] Virgil Herring analyzed 58-gm eggs in the writer's laboratory with the following results, expressed in Calories:

combustion value of the whole egg including shell	92.4
combustion value of egg less shell	90.8
combustion value of 1 gm whole, wet egg including shell	1.6
combustion value of 1 gm whole dry egg including shell	4.987
combustion value of 1 gm dry egg not including shell	6.987

It may be noted (Ch. 3) that Murray reported 6.94 Cal per gm dry egg and 5.1 to 6.1 Cal per gm dry chick; Tangl reported 1.69 to 1.73 Cal per gm dry egg. In dietetic practice it is customary to assume that the combustion value of a dozen eggs is 850 Cal, or 71 Cal per egg. Our combustion value of a 58-gm egg, namely, 90.5 Cal or 696 Cal per dozen, weighing 700 gm, is considerably higher than that computed from Chatfield & Adams' (see Table 23.1) combustion constants, namely 78 Cal per egg.

[14] Warren, D. C., and Scott, H. M., "The time factor in egg formation," *Poultry Sci.*, **14,** 195 (1935); *J. Agr. Res.*, **51,** 565 (1935). Conrad, R. M., and Scott, H. M., "Formation of the egg," *Physiol. Rev.*, **18,** 481 (1938).

perhaps a relatively small, part of the total time involved in the formation of an egg. Little is known about the time relation of yolk and germinal disk formation.[15, 16] The speed of egg production—and consequently its *gross* energetic efficiency—may not be limited by the speed of migration in the oviduct, but by the speed of maturation of the ova in the ovary. Fig. 23.1c indicates the migration of the egg in the ovary and oviduct as pictured by Mathias Duval in 1889.

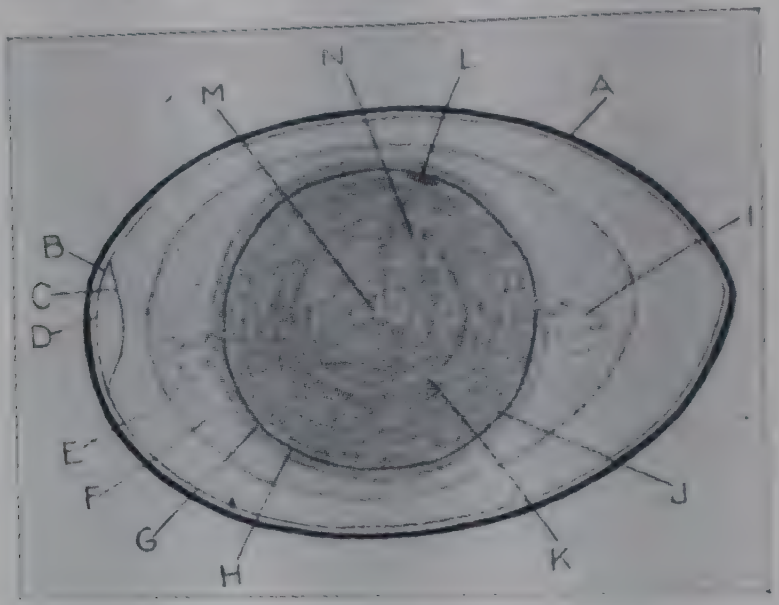

Fig. 23.1a. Structure of the egg. A, shell; B, outer shell membrance; C, inner shell membrane; D, air cell; E, outer thin portion of albumen; F, middle jelly-like portion of albumen; G, inner dense portion of albumen; H, vitelline membrane; I, chalaza; J, thin film of white yolk inside of vitelline membrane; K, layers of yellow yolk separated by thin layers of white yolk; L, germinal disk; M, central part of yolk filled with white yolk; N, slender tube connecting center of yolk with region of germinal disk. Each of these structures is in turn made up of smaller structures, as for example, the shell is composed of: (a) gelatinous outer coating; (b) outer porous layer; (c) middle granular layer; (d) inner crystalline layer; (e) inner face layer, each of different structure. The inner shell membrane is a fine cellular structure bound by many intertwining fibres; the outershell membrane coarser in structure than the inner, is also composed of fibers, and so on. (After E. W. Benjamin, Cornell Agr. Exp. Sta. Bull., 353, 1934.)

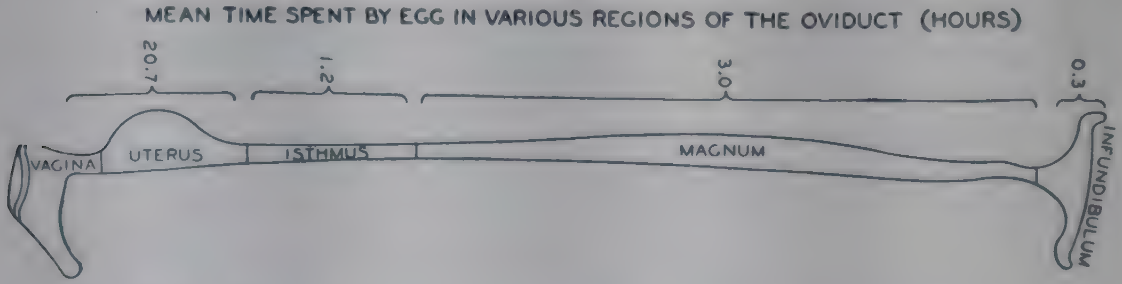
MEAN TIME SPENT BY EGG IN VARIOUS REGIONS OF THE OVIDUCT (HOURS)
20.7
1.2
3.0
0.3
VAGINA
UTERUS
ISTHMUS
MAGNUM
INFUNDIBULUM

Fig. 23.1b. Time relation of migration of the egg in the domestic fowl.

Summarizing, egg as nutriment closely resembles milk as nutriment in its evolutionary, nutritional, agricultural, physicochemical, and social-economic

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[15] Rogers, C. A., *Proc. Intern. Assn. Instructors and Investigators in Poultry Husbandry*, **1**, 77 (1912), for attempts to investigate the time factor by feeding and injecting dyes.

[16] Lillie, F. R., "The development of the chick," New York, 1919; Lippincott, W. A., revised by Card, L. E., "Poultry production," Philadelphia, 1934; Jull, M. A., "Poultry breeding," New York, 1932.

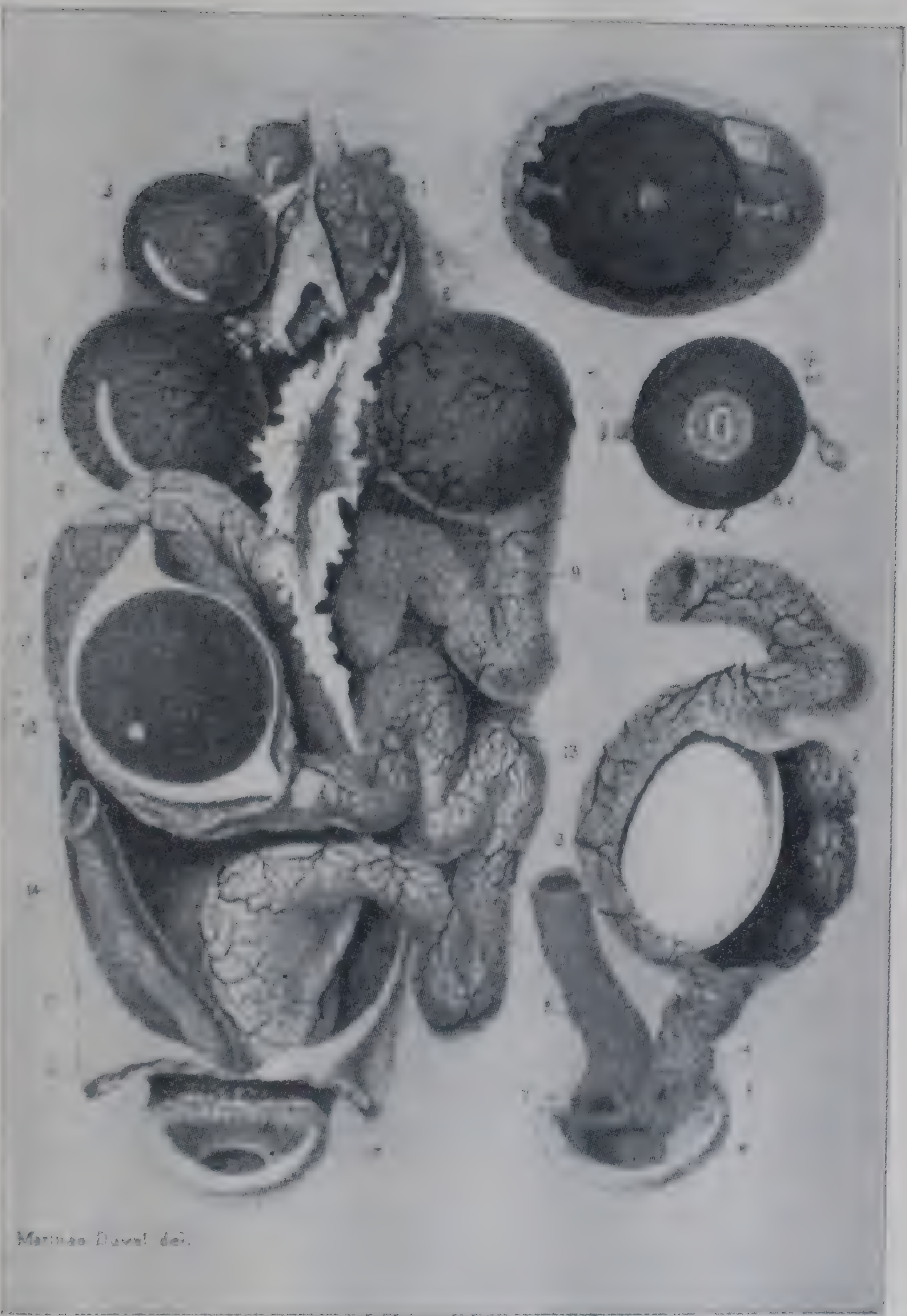

Fig. 23 1c. The migration of the egg in the ovary and oviduct as pictured by Mathias Duval in 1889. 1, ovary, with minute ovules; 2-3, yolk sacs; 4, suture line; 5, empty yolk sac, 7, funnel opening into oviduct, 8, yolk in oviduct; 9, albumen-secreting region; 10, albumen being secreted; 11, yolk passing through oviduct; 12, germinal disk; 13, isthmus; 14, uterus; 15, large intestine; 17, cloaca. On the right-hand side of the figure are shown, from the top downward: complete egg; yolk of egg incubated for sixteen hours; completed egg in uterus—(1) isthmus, (2) glands of uterus, (3) complete egg, (4) vagina, (8) cloaca.

aspects. From the standpoint of contemporary nutritional human needs, egg is richer than milk in iron, copper, vitamins D, A, and B_2, and in fat; egg is poorer than milk in calcium, sugar, nicotinic acid and vitamin C.

From the viewpoint of gross *energetic* efficiency of egg production, it is more expensive energetically to produce unit egg energy than unit milk energy for the following reasons. While the mammal might be said to dump her relatively homogeneous milk nutriment into a cistern tapped at will by the infant, the bird packages her dietary endowment to the young most elaborately (Fig. 23.1a). But it takes *time* to build an elaborate structure (Figs. 23.1b and c); and during this *time*, the builder must be maintained. Hence the *maintenance cost* is greater, and therefore gross efficiency is less for producing unit egg energy than unit milk energy. As previously noted, however, egg is not consumed for its energy content alone.

The relation between profit and energetic efficiency is somewhat similar for egg and milk production. The relation between profit and body size for egg production might be the same physiologically as for milk production; actually, for reasons which will be discussed, it is not.

In view of the similarities between egg and milk production (physicochemical, physiological, nutritional, social-economic, agricultural) the reader is referred to the detailed discussion on milk production in Chapters 21 and 22.

23.2: Energetic efficiency of egg production.[17] The energetic efficiency of egg production is evaluated by the same method as for milk production described in Section 21.6 with the aid of the following two basic equations:

Gross energetic efficiency of egg production

$$= \frac{\text{egg calories produced}}{\text{feed } (TDN) \text{ calories consumed including maintenance feed}} \tag{23.1}$$

Net energetic efficiency of egg production

$$= \frac{\text{egg calories produced}}{\text{feed } (TDN) \text{ calories consumed less } TDN \text{ expended for maintenance}} \tag{23.2}$$

If body weight and composition are assumed to remain unchanged, the gross efficiency with respect to TDN (total digestible nutrients) is computed from the equation

$$\text{Gross energetic efficiency of egg production} = \frac{1.6 \times \text{egg grams produced}}{3 \times \text{feed grams consumed}} \tag{23.1a}$$

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[17] Brody, S., Funk, E. M., and Kempster, H. L., Univ. Mo. Agr. Exp. Sta. Res. Bull. 278, 1938. Detailed numerical data are there given.

in which 1.6 and 3 are, respectively, the calorie equivalents per gram of whole egg and of assumed TDN[18] in the feed.

The *net efficiency* (not including maintenance cost) is estimated by mathematical partitioning of the feed consumed between its three uses: egg production, maintenance, and body-weight gain (or loss). The partition equation for egg production is of the same form as for milk production (Sect. 21.6):

$$\text{Feed} = B(\text{egg}) + CW^{0.73} + D\,\Delta\,W \qquad (23.3)$$

This is a statement of an energy balance between the TDN (feed) consumption on the left side, and egg production, maintenance, and weight-gain on the right side.

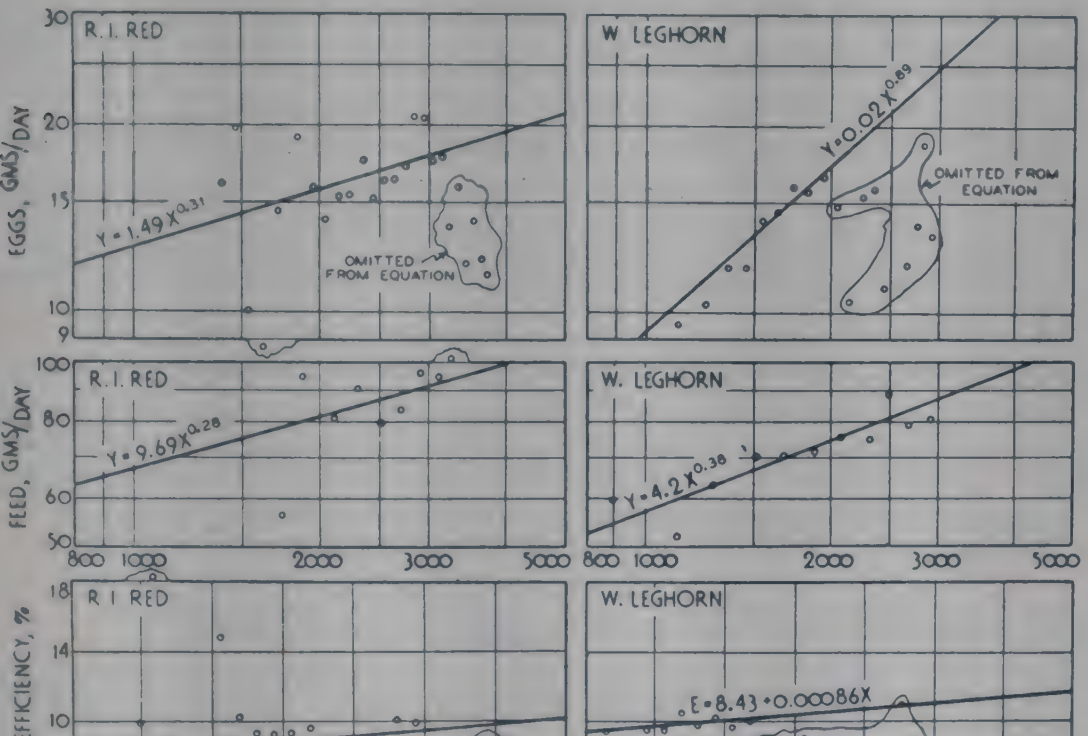

Fig. 23.2. Influence of body weight on egg (grams) production, and on feed consumption during 28-day periods and gross efficiency of egg production of our birds.

The significance of its parameters (B, C, D,) depends on the accuracy of the basic data (TDN, egg, live weight, live-weight gains), the size and homogeneity of population, range of data, and method of fitting equation to data.

We solved the equation by the method of least squares, which determines the values of B, C, and D so that the sum of the squares of the differences between observed TDN and TDN computed from this equation is a minimum. The solution consists, as explained in Section 21.6.5, in substituting in three "normal equations," and simultaneously weighting the trends of TDN with each of the other three variables (egg, W, ΔW) in such manner as to give a minimum value for the sum of the squares of the differences.

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[18] The TDN was estimated from Morrison's tables in his "Feeds and Feeding" without implying, however, that it is appropriate to estimate TDN for chicken feeds from these tables. The use of TDN values, even if of a makeshift nature, is necessitated by our comparative viewpoint, as for comparing efficiencies of egg and milk production.

The partition equation (23.3) was fitted to 2237 of 28-day periods (Fig. 23.2) with the following results:[17]

$$\text{Feed} = 0.692\ (\text{egg}) + 0.300W^{0.73} + 1.07\ \Delta W \tag{23.4}$$

which indicates that 0.692 gm feed was expended for producing 1 gm whole egg (including shell); 0.30 gm feed was expended to maintain $W^{0.73}$ gm body weight; and 1.1 gm feed was expended for changing body weight by 1 gm. We assumed that the same amount (but of different sign) of feed was involved in gaining or losing unit body weight. This assumption is subject to criticism. Since, however, the fraction of the feed used for body weight changes is relatively insignificant, the assumption was perhaps justified in the interest of simplified computations.

The *net efficiency*, that is, the ratio of egg calories produced to TDN consumed above the maintenance and weight-gain cost, is therefore given by the relation

$$\text{Net efficiency of egg production} = \frac{\text{gm egg produced} \times 1.6}{\text{gm feed consumed for eggs} \times 3}$$

$$= \frac{1 \times 1.6}{0.692 \times 3} = 0.77 \text{ or } 77\%$$

(1.6 is the caloric value of a gram egg; 3 is the caloric equivalent of TDN in a gram feed.)

The above numerical result means that under the given condition, out of 100 Cal. TDN consumed *above maintenance and above live weight changes* as computed by us, 77 Calories were recovered in the eggs, and the remainder expended for the cost of various intermediate transformations. It may be recalled that the *net* efficiency of milk production with respect to TDN in 243 experiment-station cows was computed to be 62 per cent. The difference between 62 and 77 per cent in *net* efficiencies of milk and egg production appears to be within the limits of variability of the data and equation constants.[19]

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[19] Theoretically equations (23.3) and (23.4) should have an additional parameter constant A, thus:

$$TDN = A + B\ (\text{egg}) + CW^{0.73} + D\ \Delta W \tag{23.5}$$

Fitting this equation to the data by the method of least squares resulted in the equation

$$\text{Feed} = 7.77 + 0.688\ (\text{egg}) + 0.273\ W^{0.73} + 1.09\ \Delta W \tag{23.6}$$

the constants of which do not differ substantially from those in equation (23.4). The standard error of estimate of equation (23.4) is 17.70 and of equation (23.6) is 17.71; the index of correlation of equation (23.4) is 0.722, and of equation (23.6) is 0.724, indicating that leaving out the parameter constant does not appreciably alter the situation.

A computation in the following section indicates that the net efficiency of egg production is only 54 per cent.

The *net* energetic efficiency thus appears to be of the same order for egg as for milk production; that is, the energetic efficiency of transforming *TDN* into eggs when maintenance cost is not included is of the same order as the efficiency for milk production when maintenance cost is not included. It is therefore concluded that the *ovary and oviduct produce egg from egg precursors with the same energetic efficiency as the mammary gland produces milk from milk precursors.*

It is emphasized that *gross* efficiency is simply the ratio of energy in eggs produced to energy in *TDN* consumed (assuming 1 gm *TDN* has an energy content of 4 Calories); no assumptions are involved in estimating gross efficiency except that the body weight and body-composition remain unchanged, or are properly corrected for. Net efficiency is, on the contrary, quite involved. The numerical value of net efficiency is dependent not only on the reliability of the basic data (egg energy produced, *TDN* energy consumed, gain or loss in live weight) but also on the number of birds included in the computations, range in live weight and egg production, homogeneity with regard to relative inherited capacities for egg production, fattening, maintenance-need levels, etc.

Instead of expressing net efficiency in the form of percentage energy in the egg produced to the assumed *TDN* energy in the feed consumed above maintenance, it may be expressed in the more familiar terms of feed consumed above maintenance per egg or dozen eggs produced. Thus from equation (23.4):

0.692 gm feed is consumed above maintenance for producing 1 gm egg
or 0.692 lbs " " " " " " " 1 lb "

since 1 egg weighs about 2 oz, or $\frac{1}{8}$ lb. Therefore

$0.692 \times \frac{1}{8} = 0.0865$ lb feed is consumed above maintenance for producing 1 egg;

or

$0.0865 \times 12 =$ *1.04 lb feed is consumed above maintenance for producing a dozen 2-oz eggs.*

Since 2 oz is equivalent to about 57 gm,

$0.692 \times 57 =$ *39.5 gm feed is consumed above maintenance for producing 1 egg weighing 2 oz or 57 gms.*

After our original report[17] was published, our attention was called[20] to the fact that, employing a different method, Titus[21] reported that "the amount of this special feed mixture required over and above the maintenance requirement to produce an egg was estimated as being about 40 grams." It is of course gratifying that a practically identical result (40 as contrasted to our 39.5) was obtained independently on other data by another method.

Notes on the data. The data on feed consumption, egg production, body weight, and body-weight gains analyzed above were secured on a total of 289 birds, 174 White Leghorns and 115 Rhode Island Reds, during the course of three years (1934-7). A total of 2524 28-day observations were made, including 1429 periods on White Leghorns and 1095 periods on Rhode Island Reds. However, some of the periods were incomplete and were omitted, with the result that the following efficiency computations are based on 2237 28-day periods.[17]

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[20] Titus, H. W., "Food and Life", Yearbook of Agriculture, U. S. D. Agriculture, Washington, p. 802, 1939.

[21] Titus, H. W., "The gross maintenance requirement of White Leghorns," *Poultry Sci.*, **8**, 80 (1928–9).

The birds were kept in individual compartments in laying batteries. Each compartment was supplied with a feeding box containing the following all-mash mix:

	lbs. *TDN**
Ground corn, 35 pounds	29.3
Ground wheat, 20 pounds	15.68
Ground oats, 15 pounds	10.73
Wheat bran, 10 pounds	7.02
Alfalfa leaf meal, 5 pounds	2.85
Meat scraps, 8 pounds	5.46
Dried butter milk, 5 pounds	4.28
Cod liver oil, 1 pound	1.14
Salt, 0.05 pound	
Finely ground limestone, 2.0, pounds	
Total, 101.5 pounds	76.47

* Morrison's Conversion Tables.

We assumed that 1 gm *TDN* has an energy value of 4 Calories, or 1 pound *TDN* 1814 Calories. By this assumption 1 gm of this feed mix was computed to be equivalent to 3 Cal *TDN*, or 1360 Cal *TDN* per pound of feed. Future computations in this chapter will be made with reference to feed consumed, equivalent to 3 Cal *TDN* per gm feed or 1360 Cal *TDN* per pound feed.

The energy value of eggs was found by analyzing a dozen No. 1 (58 gm) eggs.[13] The fuel value of the egg was found to be 1.6 Cal. per gram whole egg including shell.

Our data are unsatisfactory in several respects. The housing was very poor—too hot in the summer, too cold and drafty in the winter—with resulting unsatisfactory health and production of the birds. Of course, the lower the production level the greater the maintenance cost per egg produced, and consequently the lower the *gross* energetic efficiency; but this may not influence seriously the *net* efficiency. This situation explains in part the unusually low gross efficiency level of egg production of this group of birds, as will be explained presently.

23.3: Influence of live weight on gross efficiency of egg production. The following table (on New Hampshire Red pullets) indicates the method employed for computing gross efficiency of egg production. The complete data are given in the original report.[17]

Date of 28-day period	No. of birds in group	Ave. live wt. (gm)	Ave. daily live wt. gain	Eggs per bird per period	Average daily egg production			Ave. daily feed consumption		% energetic efficiency not corrected for weight gains
					gm/day	Cal./day	% possible production	gm/day	*TDN* (Cal./day)	
10/23/37 to 11/19/37	88	2282	4.8	10.3	20.0	32.0	36.8	112.0	336.0	9.5
11/20/37 to 12/17/37	73	2419	6.9	9.3	18.8	30.1	33.2	114.6	343.8	8.7
12/18/37 to 1/14/38	71	2544	1.6	15.5	33.6	53.8	55.4	129.9	389.7	13.8

This table shows that this particular group of birds produced eggs at a gross energetic efficiency (with respect to the assumed *TDN* energy in the feed) of 9 to 14 per cent depending on the number of eggs produced during the period. As indicated in Fig. 1.1 the gross energetic efficiency of egg production rises with increasing egg production but at decreasing increments in accordance with the law of diminishing increments, approaching a gross efficiency of 15 to 35 per cent as limit, depending apparently on body weight. It appears that large fowls cannot attain as high an efficiency level as small for reasons to be discussed presently.

As is generally known, and as is illustrated in Figs. 23.3a and b, egg weight and in some cases egg number tend to increase with increasing body weight up to a certain body-weight level, following which egg number decreases. The body weight of maximum production is of the order of 4 lbs in Leghorns and 5¾ lbs in the heavier breeds, as R.I. Reds and B.P. Rocks. Fig. 23.2 shows that the production and gross efficiency levels of our birds increased up to body weight about 3000 gms (about 6 lbs) in the R.I. Reds, and 1800 gms (about 4 lbs) in the Leghorns, and then decline. The slight increase in efficiency with increasing body size up to these body-weight levels appears to be due not to body weight as such, but to improved nutritional and health conditions of the birds.

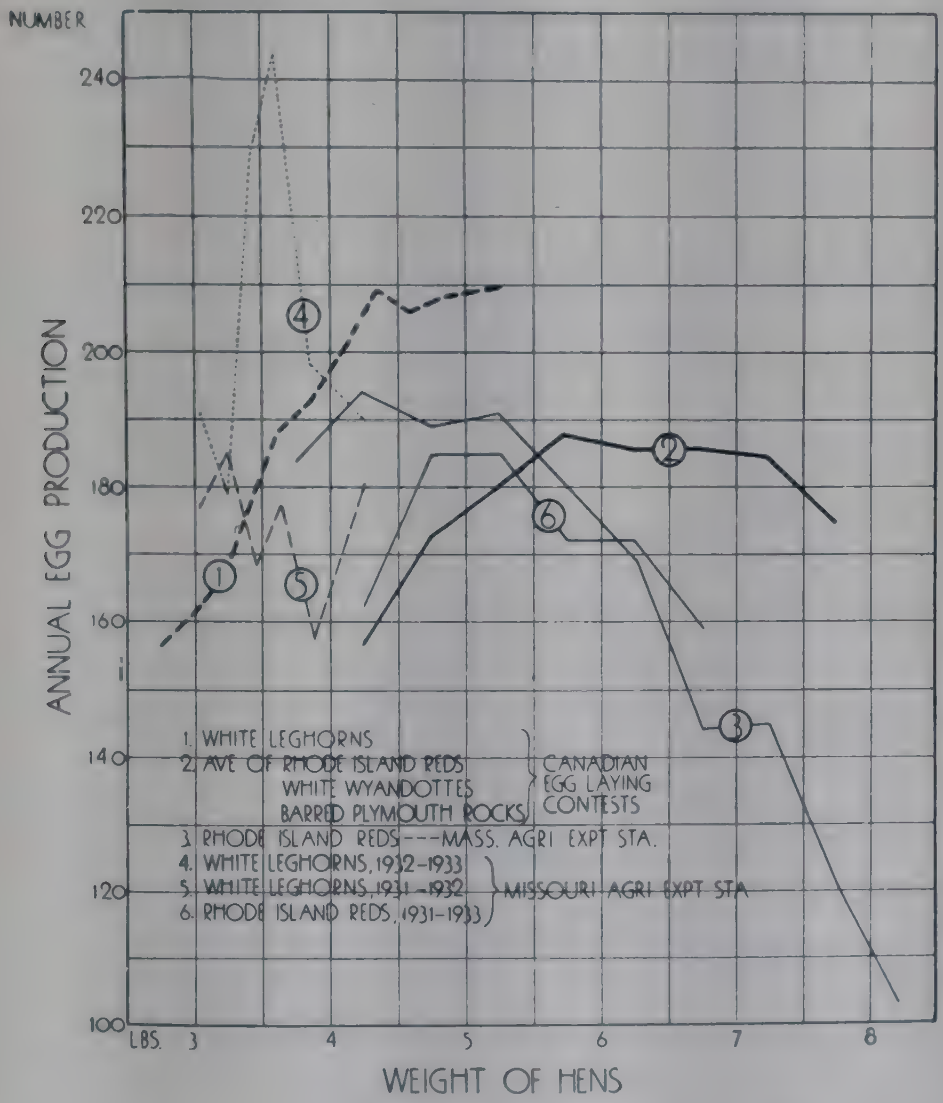

Fig. 23.3a. Rise in egg *number* per year with increasing body weight. For the sources of the Canadian egg-laying contest data see Dominion of Canada, Dept. Agr. Bull., 139, Ottawa.

It is instructive to compare the efficiency of our birds as indicated in the above discussion with those computed from data in the literature. As the published data were secured for purposes other than efficiency computations, they lack certain details which we shall have to assume. In these computations we shall assume that 1 gm whole egg is equivalent to 1.6 Calories, and 1 gm chicken feed 3 Calories *TDN* per gram, or 1360 Calories *TDN* per pound.

We may first cite data by Byerly, Titus and Ellis[23] listed in columns 1 to 4 of the following table, to which we have appended column 5 giving the computed gross energetic efficiency of the egg production. Column 5 indicates that the gross energetic efficiency of egg production of 200-egg fowls is only about 14 per cent. Some of the food, however, was used for growth, for which no correction was made.

We also computed (columns 3, 4, 6, 7 in table 23.2) the gross efficiency of egg production of the birds in seven egg-laying contests in Utah.[24]

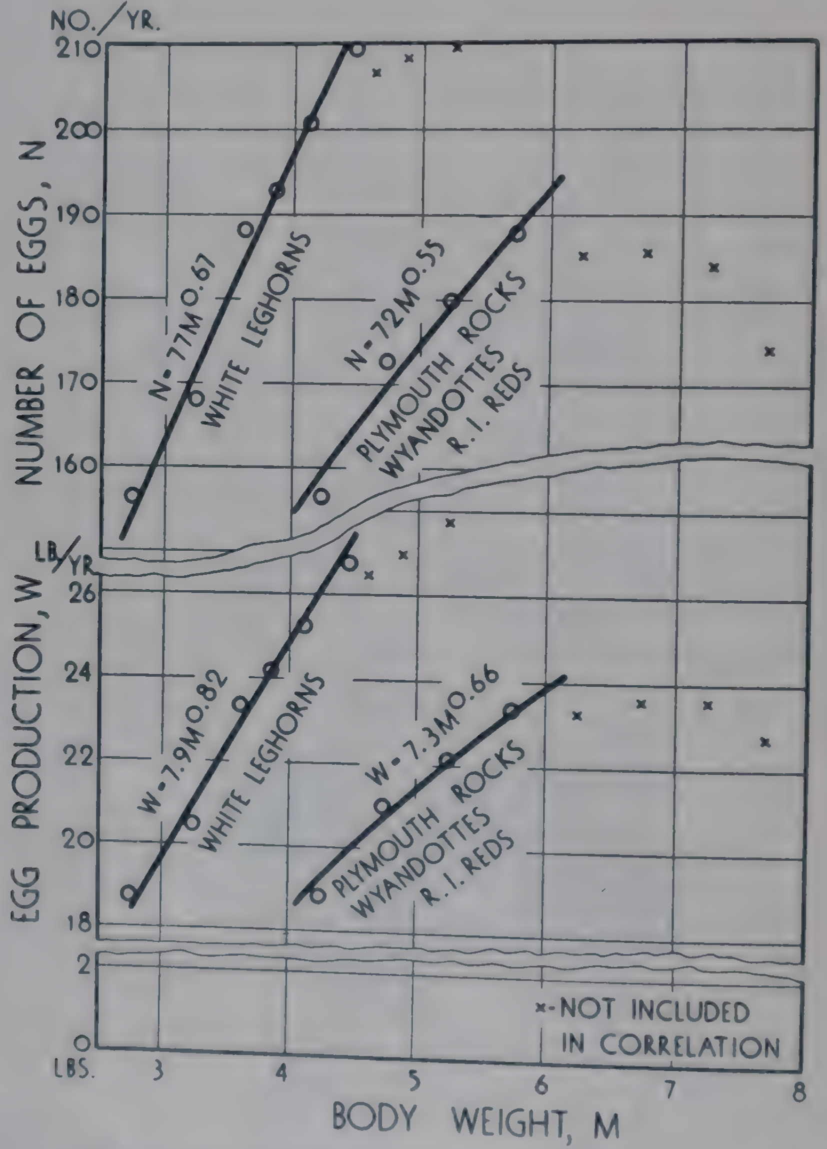

Fig. 23.3b. Canadian-contest data continued.

These results indicate that the overall energetic efficiency of the Utah Leghorns is of the order of 17 per cent on a yearly basis, and 19 per cent for the highest production period (May–June). These 19 per cent efficiency birds may be considered to be fairly high-producing fowl, comparable to the high-producing cows for which we found an overall percentage efficiency of 33 per cent.

Waite[25] similarly summarized data for six Maryland egg-laying contests (November 1925–October 1931). We computed the gross efficiency as before. Egg weights were not given. We assumed that the eggs weighed 56 grams each. The results given in Table 23.3 indicate that the gross efficiency of egg production varies, among other factors, with the size of the birds. The larger the birds, the smaller, apparently, the gross efficiency.

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[23] Byerly, T. C., Titus, H. W., and Ellis, N. R., *J. Agr. Res.*, **46**, 1 (1933).

[24] Alder, B., Utah Agr. Exp. Sta. Bull. 248, 1934.

[25] Waite, R. H., Maryland Agr. Exp. Sta. Bull. 359, 1934.

Efficiency of Egg Production Computed from Byerly, Titus and Ellis

Diet No.	Eggs produced per gram of feed eaten after average date of 1st egg	Egg/hen per pullet year	Change in body weight (gm)	Gross energetic efficiency* (not corrected for change in body weight)
1	0.229	197.0	316	12.2
2	0.212	187.5	252	11.3
3	0.231	188.1	341	12.3
4	0.205	168.0	358	10.9
5	0.172	145.8	−15	9.2
6	0.219	173.0	296	11.7
7	0.191	159.5	81	10.2
8	0.251	204.5	365	13.4
9	0.198	157.8	—	10.6

* Column 5 was computed on the assumption that 1 gm feed is equivalent to 3 Cal., and 1 gm egg to 1.6 cal. Thus $\frac{0.229 \times 1.6 \times 100}{1 \times 3} = 12.2$ per cent. The data are based on a 344-day period (Sept., 1929 to Aug., 1930).

Summarizing, the yearly gross energetic efficiency of egg production with respect to the assumed *TDN* consumed varies greatly, the maximum of "good" layers being of the order of 19 per cent. It appears that above a certain body-weight level efficiency tends to decrease with increasing size of birds.

23.4: Influence of production level on gross efficiency of egg production. Fig. 1.1 (page 3), based on our data generalized by equation (23.4), represents the functional relation between gross efficiency of egg production and the production level. From this it appears that the maximum efficiency, attained on 300-egg birds, should be of the order of 25 per cent. Does efficiency of egg production actually reach this level? By way of orientation, it is profitable to examine Waite's Maryland egg-laying contest data on egg production and feed consumption of birds classified by production levels. As the egg weights are not given in Waite's report we assumed a constant egg weight of 56 grams. The energetic efficiencies of egg production of three breeds thus estimated are listed in Table 23.3a and b and charted in Fig. 23.4.

Table 23.3b and Fig. 23.4 indicate that "good" layers, good enough to be included in egg-laying contests, have a gross energetic efficiency with respect to *TDN* consumption up to at least 19 per cent. If a *pen* of birds can produce eggs at 19 per cent efficiency, it is probable that *individual* birds may reach a 25 per cent efficiency level. These data therefore substantiate the curves in Fig. 1.1 that the gross efficiency of egg production may rise to 25 per cent. (While the distribution of the data points in Fig. 23.4 is approximately linear,

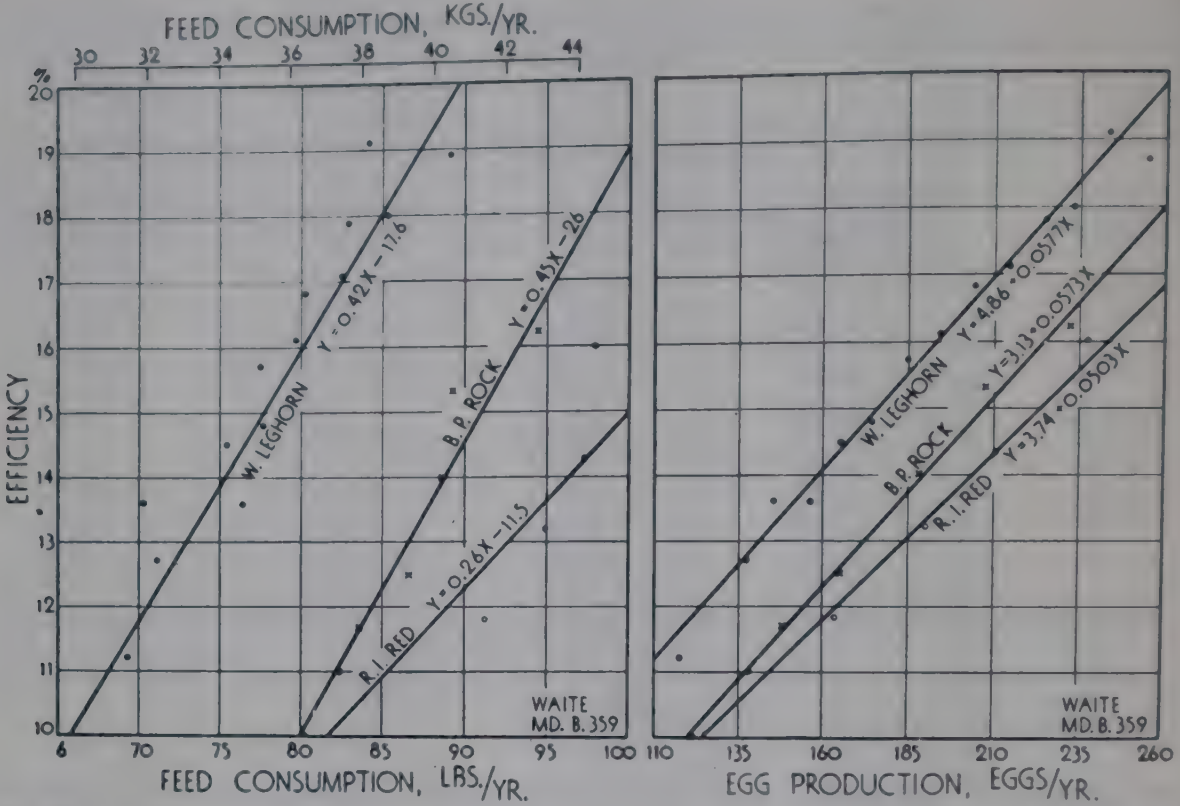

Fig. 23.4. Efficiency as function of egg production and feed consumption levels of the Maryland data.

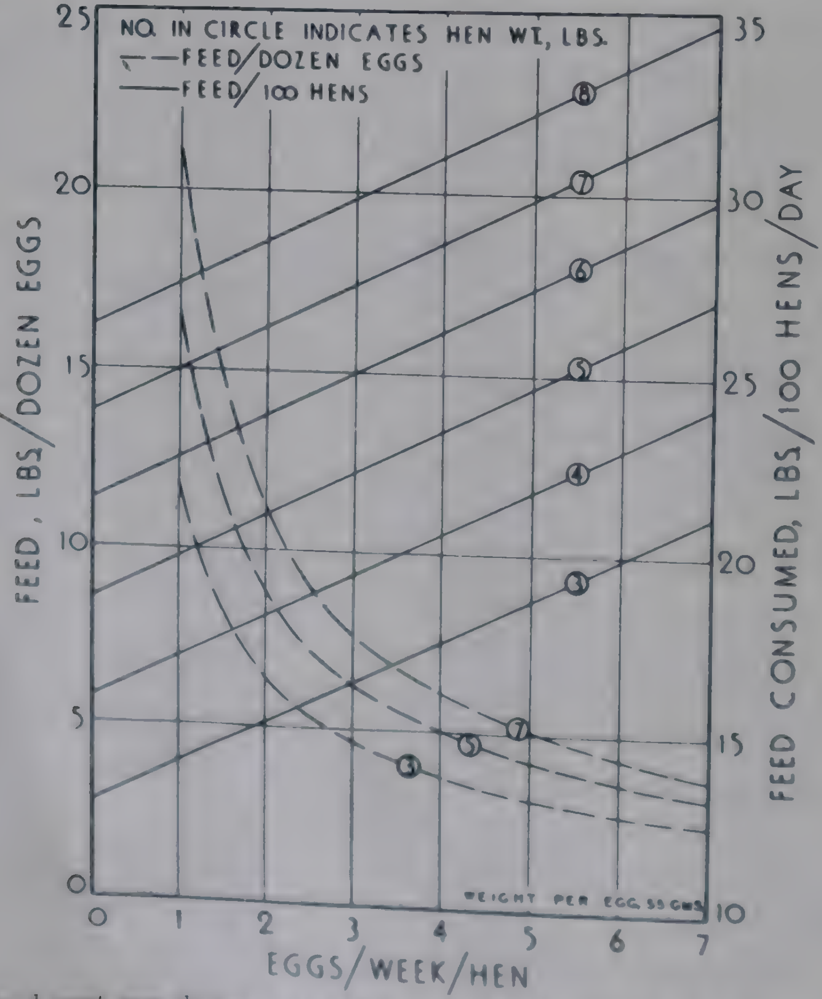

Fig. 23.5. Feed cost per dozen eggs (left axis of ordinates and declining curves) and total feed consumption per 100 fowls per day (right axis of ordinates and rising curves) for fowls of different live weight plotted from Table 23.4. The eggs were assumed to weigh 55 gm. each.

the large values of the intercepts indicate that the curves as a whole are parabolic, similar to the curves in Fig. 1.1.)

Summarizing, the energetic efficiency of egg production, like that of milk production, increases with increasing production level in accordance with the law of diminishing increments. The energetic efficiency of pens of birds at the given egg-laying competitions ranged from about 10 to 19 per cent with respect to TDN consumed. Assuming that the *net* efficiency (not counting maintenance cost) of egg production is constant (about 1 lb feed per dozen eggs) these 10 per cent differences in gross efficiency are due to differences in maintenance tax imposed on the egg. The larger the number of eggs produced, the smaller the maintenance per egg, and consequently the higher the gross efficiency.

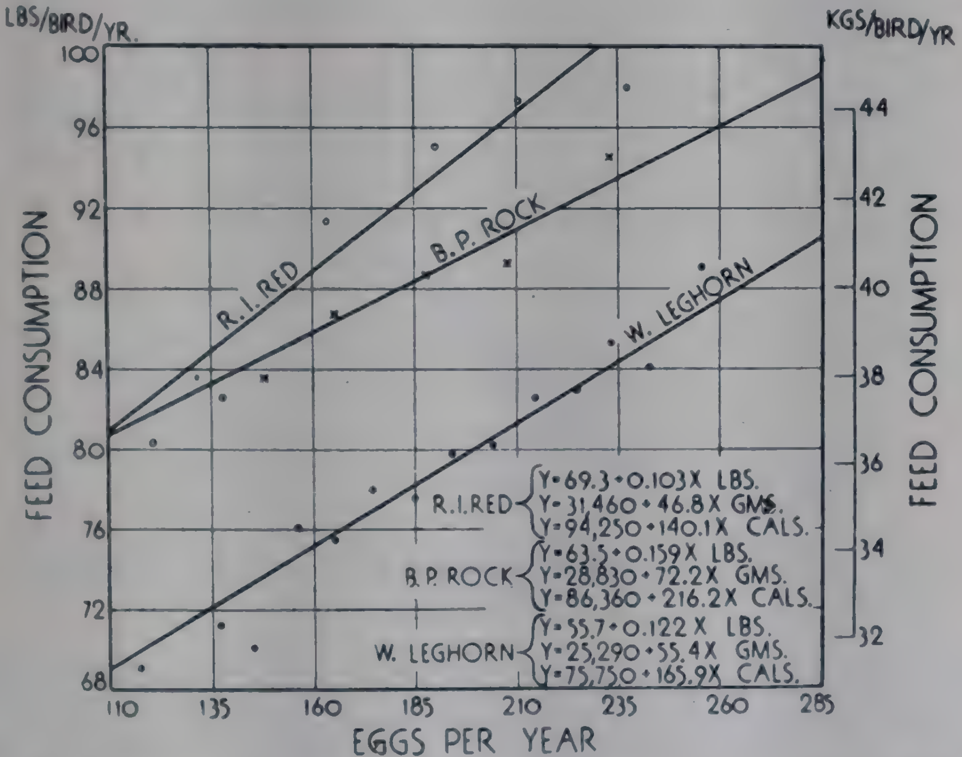

Fig. 23.6. Feed consumption as function of egg production number, based on the Maryland egg-laying competition data.

23.5: Feeding standard for poultry. From equation 23.4, the feed required for egg production is given by the equation

$$F = 0.692e \tag{23.4a}$$

and the feed required for maintenance by

$$F = 0.30W^{.73} \tag{23.4b}$$

in which F, e, and W are respectively feed, egg, and live weight in grams.

The maintenance feeding standard for chickens, computed from equation (23.4a) is given in Table 23.4 (appendix); the amount of feed required for producing egg above maintenance (about 1 lb feed for a dozen 2-oz eggs) was previously computed (Sect. 23.2). The two may be combined into one feeding standard including both feed for maintenance and production, as given in Tables 23.4 and Fig. 23.5.

The following alternate method comes to mind for estimating the feed cost of maintenance and production for the *average*-weight bird. The method is indicated in Fig. 23.6. Plot feed consumption against egg production. The resulting curve should not, theoretically, be linear (the feed consumption should, according to the law of diminishing increments, rise more rapidly than egg production) but it appears to be roughly linear; therefore fit a linear equation to the data. Consider, by way of example, the curve of the Leghorn data: its equations (in various units) show that the feed cost of *maintenance* (not counting egg production cost) of the average bird is 55.7 lbs a year (or 25.3 kg, or 76,000 Cal); that the feed cost for producing an egg (not counting maintenance) is 0.122 lbs (or 55.58, or 166 Cal). The maintenance value, 55.7 lbs feed per year, agrees with

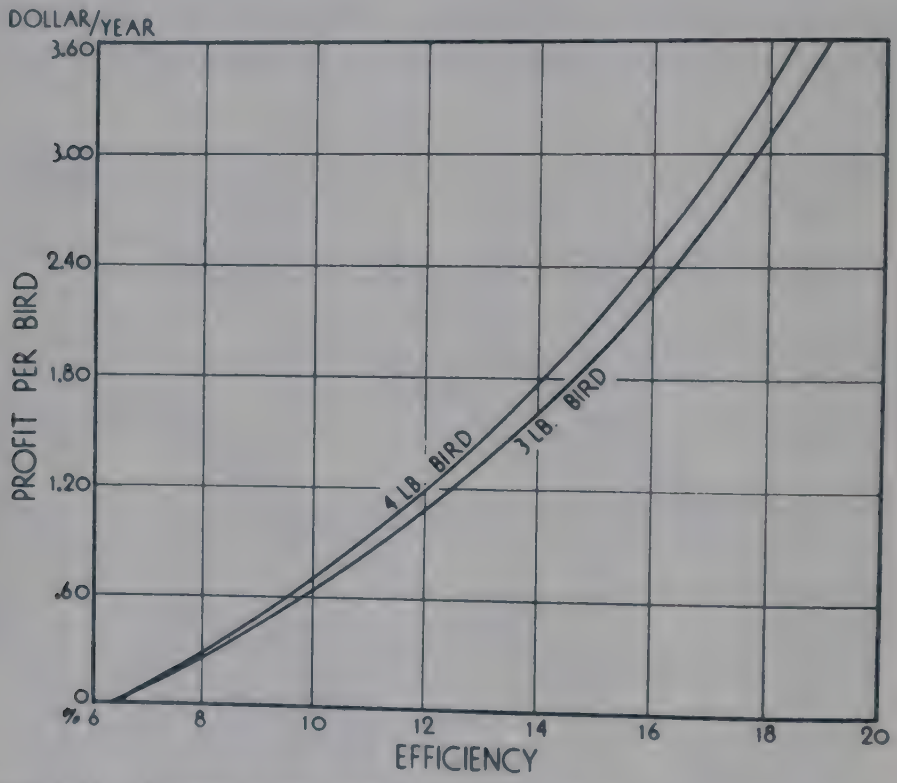

Fig. 23.7. Relation between profit and efficiency. The curves are *based on the assumption* that 56 gram eggs are sold at 25¢ a dozen and feed (containing 1360 Cal. TDN per pound) cost $2.00 per 100 lbs., and *that there was no other expense or income.* Actually, about 10 per cent of the income comes from sale of birds; and the expense for feed is perhaps only 50 per cent of the total expense which includes labor (20–25 per cent), replacement (10–20 per cent), depreciation (8–10 per cent), interest (4–5 per cent), taxes (½ per cent), etc. Note from this chart that according to these assumptions, it requires a 7 per cent efficiency to cover feed cost, and that the profit increases more rapidly than the efficiency.

the values in the feeding standard for chickens (Table 23.4) assuming that the average Leghorn chicken weighs somewhat below 4 lbs. The production value, 0.122 lbs, or 166 Cal. feed per egg is not unreasonable, because it yields a net efficiency of egg production (for a 56-gram egg) of $\frac{56 \times 1.6}{166} = 54$ per cent. This net efficiency value[27] is lower than the average obtained on our own data (77 per cent), but it is identical with the average net efficiency of milk production of 368 cows (Ch. 21), and the range in net efficiency for milk production in several groups of cows is no less than for egg production of several groups of chickens. Fig. 23.6 is, at any rate, informative, indicating at a glance the relation between feed consumption per year and egg production of several breeds of chickens. It is particularly instructive to note that for a given number of eggs produced the small birds consumed less feed than the large ones. Thus the 200-egg Leghorns consumed nearly 20 per cent less feed than the 200-egg R.I. Reds, while the R.I. Red egg is less than 5 per cent larger than the Leghorn egg. Hence the energetic efficiency of egg production is greater for Leghorns than R.I. if both produce the same number of eggs per year.

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[27] This net efficiency value was confirmed by S. Bird and J. W. Sinclair, *Scientific Agr.* **19**, 542 (1939), who reported 62% net efficiency.

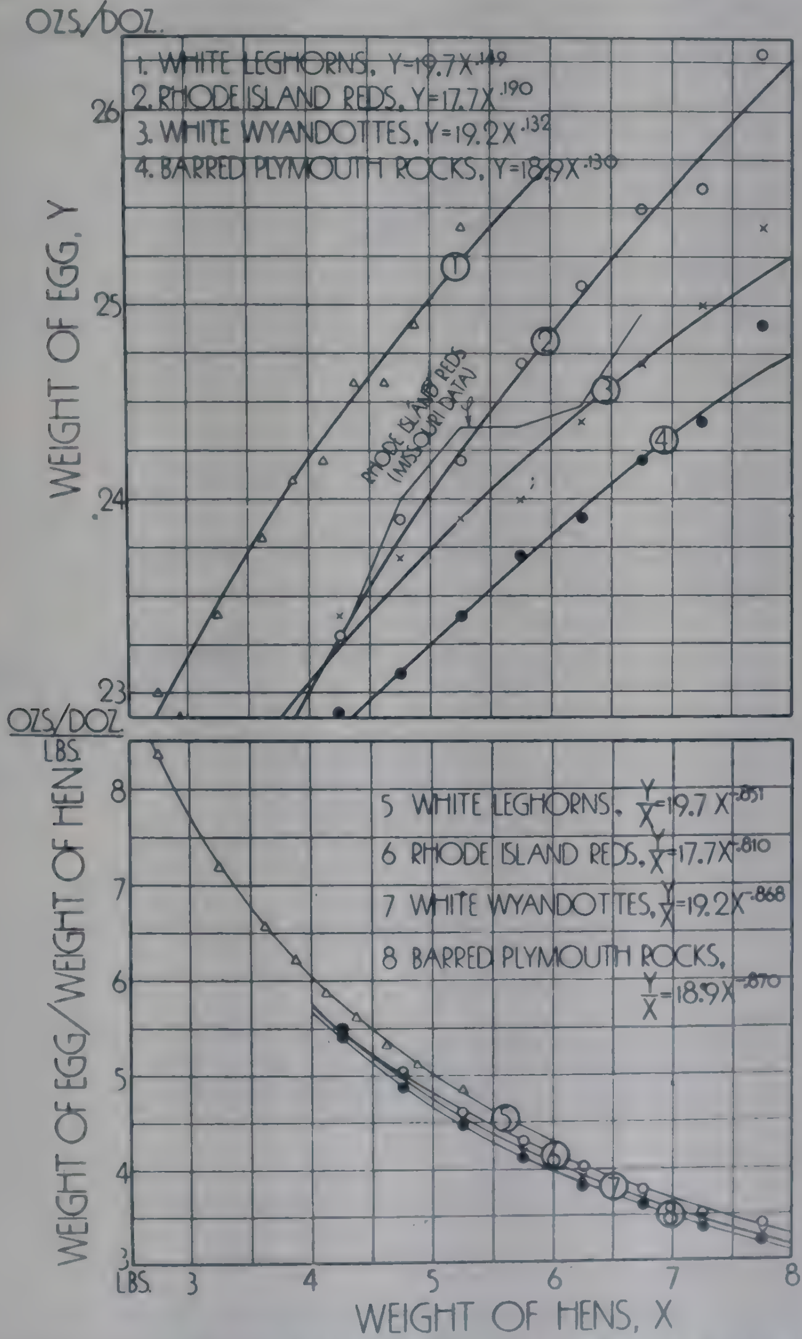

Fig. 23.8a. The relation between weight of egg and weight of fowl within the species. The equation indicates that a 100 per cent increase in body weight is associated with a 13 per cent to 19 per cent differential increase in egg weight. Note from Figs 23.9 and 15.6 that for mature birds of *different species*, the egg weight increases not by 13 per cent to 19 per cent but by 60 per cent to 70 per cent, at the same rate as the maintenance cost increases.

23.6: Interrelation between profit, gross efficiency of egg production, body size, and egg size. Fig. 23.7 indicates the relation of profit to gross efficiency of egg production; a relation similar to that for milk production (Fig. 22.4a).

The biologic unit of egg production is, of course, not the pound or calorie of egg, but the individual egg. Consequently, one would not expect an in-

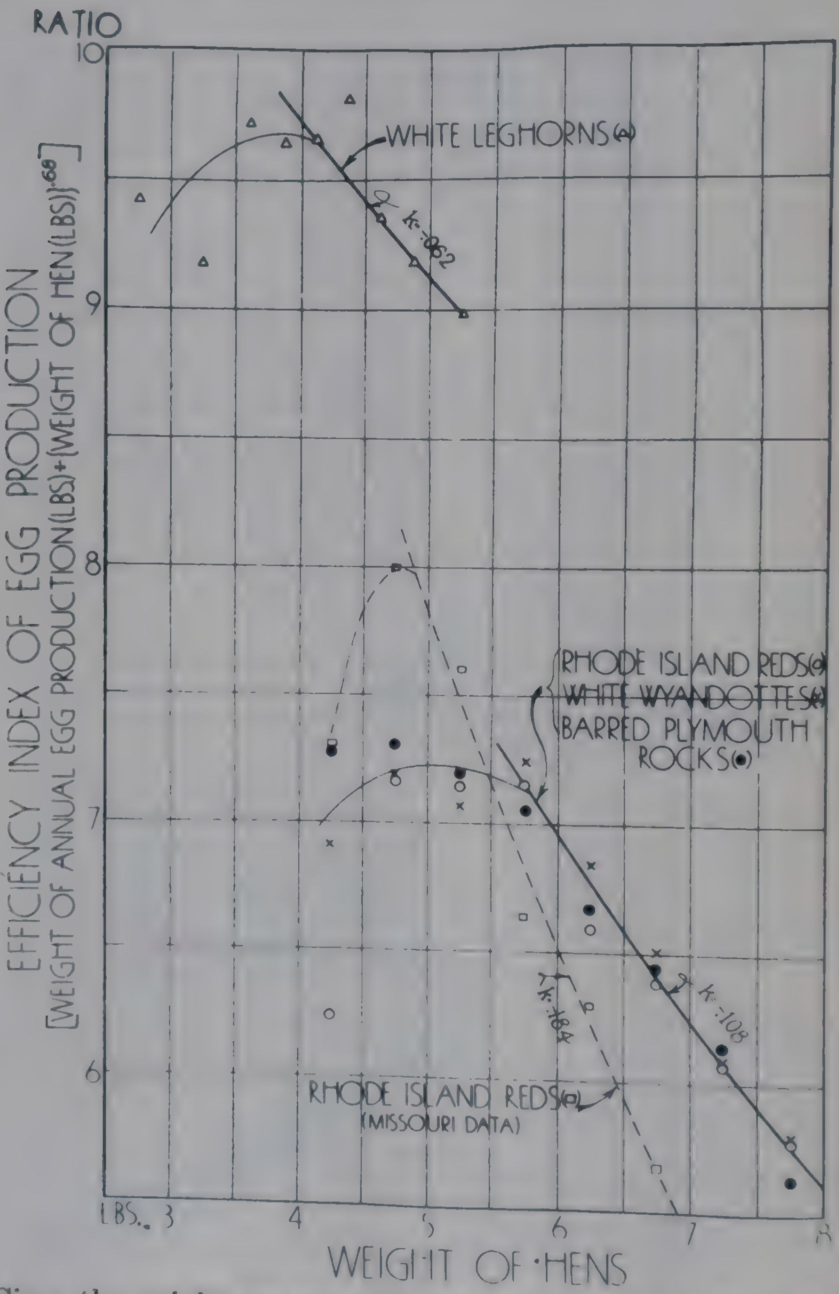

Fig. 23.8b. Since the weight per egg does not increase as rapidly as the maintenance cost with increasing body size, the gross efficiency of egg production must decline (if egg *number* is the same). This chart shows that, following a certain optimum body weight, the gross efficiency indeed declines with increasing body weight at the differential rate of 6 per cent (W. Leghorn) to 18 per cent (R. I. Red) per pound increase in body weight.

crease in *egg number* but in *egg size* with increasing body size; and, as demonstrated in Fig. 15.6, egg size of mature birds of *different species* increases, on the average, with the 0.73 power of body weight, as does basal metabolism, and probably maintenance cost. Within the species, however, for chickens of different body weight egg size increases not with the 0.73 but with the 0.15

power of body size. It follows from this 0.15 power rise in egg size, that if maintenance cost of chickens increases with the 0.73 power of body weight, and egg number remains constant, the energetic efficiency of egg production decreases with increasing body size.

This situation is similar to the one we met in the tendency for the gross efficiency of milk production to decline with increasing live weight (Sect. 21.6.4) and for a similar reason: the tendency to select in breeding such small birds as produce relatively large eggs. The difference in egg size from small and large fowl is not sufficient to pay for the differences in cost of maintaining small and large fowl, especially if the small fowl is a Leghorn and the large fowl is, for example, a Barred Plymouth Rock belonging to the strain represented in Fig. 23.8a (which shows that the egg weight from a 7-lb Barred Plymouth Rock is the same as that from a $4\frac{1}{4}$ lb Leghorn).

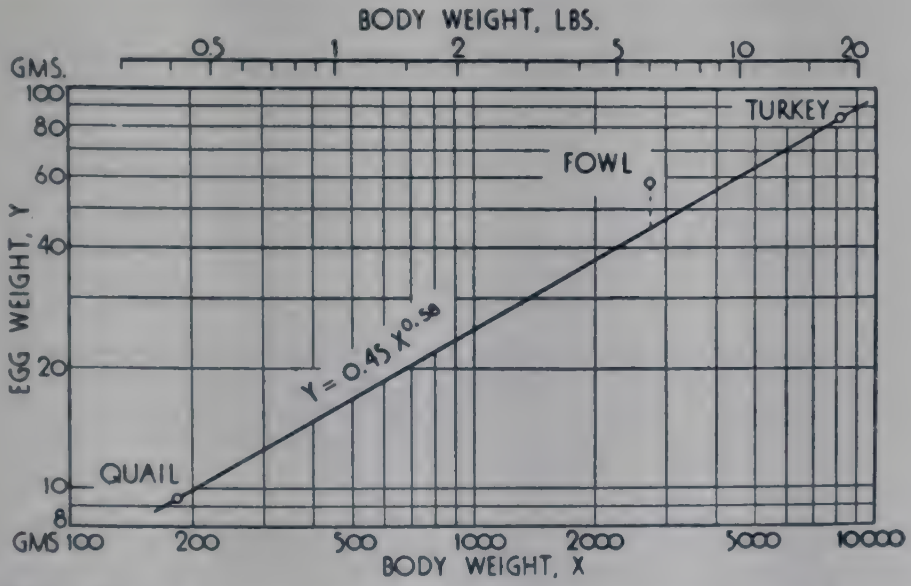

Fig. 23.9. While Fig. 23.8a shows that in the *same species* and breed the egg production rises only 13 per cent to 19 per cent for an increase in body weight of 100 per cent, this chart shows that for closely related but different species—quail, fowl, turkey—the egg size increases 58 per cent for an increase in body weight of 100 per cent.

23.7: Summary. Eggs resemble milk in most respects (evolution as food for young, composition, nutritional value, physicochemical and endocrine mechanisms), and differ in few, especially in concentration of carbohydrate, fat, calcium, iron, copper, and vitamin C.

The *gross* energetic efficiency of egg production is below that for milk production, because of differences in time relations of the two processes, but the *net* efficiency, not involving the time element, is of the same order for milk and egg production, indicating similar efficiency of mammary gland and ovary oviduct systems as energetic transformers.

The feed cost above maintenance for producing average (2-oz) eggs, is of the order of 1 lb feed for a dozen eggs, or 40 gms feed per egg. The maintenance cost of 100 birds per day is: for 2-lb birds, 9.5 lbs feed; for 3-lb birds, 12.8 lbs feed; for 4-lb birds, 15.8 lbs feed; for 5-lb birds, 18.6 lbs feed; for 6-lb birds, 21.3 lbs feed; for 7-lb birds, 23.8 lbs feed, and so on as given in Table 23.5. A feeding standard is presented for birds of different weights producing at different levels. No alignment charts are given for profit on egg production production as were given for milk production (Univ. Missouri Agr. Exp. Sta., Res. Bull. 239), because such charts were published by Card[28] and Byerly.[29]

23.8. APPENDIX.

Table 23.1a. Egg Nutrients per Pound, as Purchased.
(A pound is equivalent to eight eggs or a pint of milk.)

Food	Cal.	Protein (gm)	Fat (gm)	C.H. (gm)	Vitamin A (I.U.)	Thiamine (mg)	Riboflavin (mg)	Nicotinic acid (mg)	Ascorbic acid (mg)	Fe (mg)	Ca (mg)	P (mg)
Egg	635	52	46	3	4040	0.83	1.45	0.2	0	10.9	218	848
Milk	360	16	21	25	1020	0.11	0.74	0.4	4	0.9	556	427
Meat	1120	65	95	2	120	1.87	0.77	22.9	3	9.8	41	719

Table 23.1b. Nutrients per 100-Calorie portions of egg and milk.

	Weight															Calories from		
	(gm)	(oz)	Water (gm)	Protein (gm)	Fat (gm)	C.H. (gm)	Ca (gm)	P (gm)	Fe (gm)	A (I. U.)	B_1 (mg)	B_2 (mg)	C (mg)	D (I. U.)	Protein	Fat	C. H.
Edible part:																	
hen egg	63	2.2	42	9.3	6.6	—	.042	.113	.0019	600–3000	.045–.075	.2–.13	—	90–110	38	62	
egg white	181	6.4	156	23.5	0.5	—	.021	.025	.0002	—	—	.3–.6	—	—	97	3	
egg yolk	26.6	.9	13	4.2	8.9	—	.036	.139	.0023	500–1600	.05 –.09	.1–.5	—	40–130	17	83	
Cow milk	148	4.9	129	4.9	5.9	7.4	.167	.129	.0003	220– 870	.09 –.18	.1–.5	3–7	3– 30	119	52	29
Cow milk evaporated	59	2.1	40	5.8	5.4	6.3	.189	.146	.0004	200– 300	.018–.024	.2	—	—	24	50	26

Table 23.1c. Nutrients per 100-gram portion of egg and milk.

	Approx. egg wt. (gm)	Per cent										Fuel Value		Vitamins per 100 gm.				
		Shell	Solids	Water	Protein	Fat	C.H.	Ash	Ca	P	Fe	Cal/lb	Cal/gm	A (I.U.)	B_1 (mcg)	B_2 (mcg)	C (mg)	D (I.U.)
Edible part:																		
hen egg	57		26	74	12.8	11.5	0.7	1.0	.067	.18	.003	715	1.58	1000	150	300	0	150
duck egg			29	71	13.1	14.3	0.8	1.0				835	1.84				0	
goose egg			30	70	13.9	13.3	1.3	1.1				820	1.80				0	
turkey egg			27	73	13.1	11.8	1.5	0.8				750	1.65				0	
hen egg yolk			51	49	16.3	31.9	0.7	1.7	.137	.53	.0086	1610	3.55	3000	400	400	0	180
hen egg white			12	88	10.8	0	0.8	0.6	.015	.014	.0001	210	0.46	0	0	250	6	—
As purchased:																		
hen egg		11										635	1.40					
duck egg		11										745	1.64					
goose egg		13										710	1.57					
turkey egg		12										660	1.46					
Cow milk			13	87	3.5	3.9	4.9	0.7	.12	.09	.00024	315	.69	200	36	170	2	20
Cow milk evaporated			26	74	7.0	7.9	9.9	1.5	.25	.20	.0005	640	1.4	450	60	320	2	40

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[28] Card, L. E., "The application of nomographic methods in the field of poultry husbandry." *Poultry Sci.* **9**, 27 (1929).

[29] Byerly, T. C., "Breeding for hatchability." U. S. Dept. Agr. Conf. Nat. Poult. Impr. Plan, p. 61, 1936.

Table 23.1d. Composition of Eggs of Nine Species.*

Species	Egg Weight (gm)	Percentages Yolk	Albumen	Shell membrane	Shell
Turkey	81.8	31.79	57.74	1.61	8.87
Chicken	55.8	30.84	59.06	0.63	9.46
Silver pheasant	44.1	39.56	48.70	0.68	11.07
Ring-necked pheasant	26.7	32.67	56.83	0.83	9.68
Quail	10.3	30.66	59.77	2.61	6.96
Brewer's blackbird	4.6	19.86	72.70	0.66	6.77
Mockingbird	4.1	17.80	74.39	0.73	7.07
Tricolored red-wing	3.7	20.44	71.93	0.82	6.81
Barn swallow	1.9	27.36	64.74	—	7.89

*[From V. S. Asmundson, G. A. Baker, and J. T. Emlen, *The Auk*, **60,** 37 (1943).]

Table 23.2. Efficiency of Egg Production Computed from Data on the Utah S.C.W. Leghorns.

Month	Grain (lbs/month)	Mash (lbs/month)	Total (lbs/month)	Feed Calories per month	No. eggs per month	Egg Calories per month	Overall energetic efficiency
Nov.	3.54	2.45	5.99	8158	13.8	1148	14.1
Dec.	3.73	2.29	6.02	8199	13.5	1123	13.7
Jan.	3.88	2.35	6.23	8485	15.4	1281	15.1
Feb.	3.51	2.54	6.05	8240	17.4	1448	17.6
March	3.99	3.09	7.08	9643	20.8	1731	18.0
April	3.73	3.27	7.00	9534	20.1	1672	17.5
May	4.02	3.11	7.13	9711	22.0	1830	18.8
June	3.83	2.76	6.59	8976	20.6	1714	19.1
July	3.69	2.89	6.58	8962	19.7	1639	18.3
Aug.	3.52	2.27	5.79	7886	17.6	1464	18.6
Sept.	3.50	1.90	5.40	7355	15.3	1273	17.3
Oct.	3.14	1.38	4.52	6156	11.7	973	15.8
Total	44.1	30.1	74.4	101305	207.9	17296	Ave. 17.0
Column	1	2	3	4	5	6	7

Table 23.3a. Efficiency of Egg Production Computed from Waite's Maryland-Competition Data.

Breed	No. birds as No. "hen years"	Egg production per year	Feed Consumption per bird per year (lbs)	Lbs. feed consumed/doz. eggs	Gross energetic efficiency of egg production (%)
S.C.W. Leghorns	4781.2	201.1	80.5	4.8	16.5
R.C. Brown Leghorns	10.5	148.0	61.3	5.0	15.9
Ancona	57.1	162.0	73.4	5.4	14.5
Black Leghorns	11.4	144.6	66.0	5.5	14.4
Barred Plymouth Rocks	459.0	188.3	88.7	5.7	14.0
White Plymouth Rocks	49.4	146.1	83.7	5.7	11.5
Australorp	21.7	180.2	88.4	5.9	13.4
R.I. Red	655.6	181.0	92.2	6.1	12.9
S.C. Buff Leghorns	10.7	121.8	63.8	6.3	12.6
Lamona	9.7	137.4	74.4	6.5	12.2
Dominique	90.2	134.0	74.6	6.7	11.8
Silver L. Wyandotte	11.5	151.9	84.7	6.7	11.8
S.C.R.I. White	33.0	149.4	84.6	6.8	11.6
Andalusian	21.1	139.6	79.8	6.9	11.5
Wt. Wyandotte	42.9	138.9	81.0	7.0	11.3
S.C.W. Minorca	10.4	127.4	80.5	7.6	10.4
Buff P. Rock	10.7	116.3	78.4	8.1	9.8
Mottled Brahma	10.9	113.2	77.2	8.2	9.7
Black Langshan	10.2	113.3	85.5	9.1	8.7
Jersey Black Giant	9.0	93.3	84.0	10.8	7.3

Notes: In Waite's bulletin the feed values are carried to three decimals, which we abbreviated to one decimal; the egg production is carried in the bulletin to two decimal places which we abbreviated to one place. No egg weights were given. The eggs were assumed to weigh 56 grams.

$$\text{Efficiency} = \frac{\text{egg gms.} \times 1.6}{\text{feed lbs.} \times 1360}$$

Table 23.3b. Efficiency of Egg Production as Function of Production Level.

Production level eggs per year	No. birds as No. "hen years"	Ave. weight of bird (lbs)	Feed consumed per bird (lbs/year)	Feed consumed per doz. eggs (lbs)	Energetic efficiency (%)
White Leghorns					
117.7	8.2	3.61	69.30	7.06	11.2
137.3	10.1	3.40	71.10	6.21	12.7
145.1	63.3	3.21	70.28	5.81	13.6
156.5	133.4	3.60	76.04	5.83	13.6
165.5	124.0	3.54	75.40	5.47	14.5
174.6	301.4	3.55	77.90	5.35	14.8
185.0	247.1	3.57	77.58	5.03	15.7
194.3	345.7	3.49	79.70	4.92	16.1
204.5	326.5	3.56	80.25	4.71	16.8
214.8	203.8	3.58	82.53	4.61	17.1
225.0	272.3	3.62	82.98	4.43	17.8
233.2	770.1	3.76	85.32	4.39	18.0
243.0	105.9	3.77	84.02	4.15	19.1
255.8	11.4	3.81	89.15	4.18	18.9
Rhode Island Reds					
121.4	29.9		80.3	7.94	10.0
138.1	771.7		82.5	7.16	11.0
163.9	127.5		91.4	6.69	11.8
190.2	175.0		95.0	5.99	13.2
210.7	133.4		97.2	5.53	14.3
237.6	66.5		97.9	4.95	16.0
Barred Plymouth Rocks					
148.4	10.4		83.6	6.76	11.7
165.2	139.0		86.7	6.30	12.5
188.4	161.7		88.7	5.65	14.0
207.7	79.7		89.3	5.16	15.3
232.8	57.3		94.5	4.87	16.2

Table 23.4. Feeding Standard for Poultry.
A. In grams feed, or *TDN*, per fowl per day

No. eggs per week	Body weight, grams													
	1000	1200	1400	1600	1800	2000	2200	2400	2600	2800	3000	3200	3400	3600
	Feed													
0	50.1	56.1	61.8	67.4	72.7	77.9	83.0	87.9	92.7	97.4	102.1	106.6	111.1	115.5
1	55.4	61.4	67.2	72.8	78.1	83.3	88.3	93.3	98.1	102.8	107.4	112.0	116.5	120.9
2	60.8	66.8	72.6	78.1	83.5	88.7	93.7	98.7	103.5	108.2	112.8	117.4	121.8	126.2
3	66.2	72.2	78.0	83.5	88.9	94.0	99.1	104.0	108.8	113.6	118.2	122.7	127.2	131.6
4	71.6	77.6	83.3	88.9	94.2	99.4	104.5	109.4	114.2	118.9	123.6	128.1	132.6	137.0
5	77.0	83.0	88.7	94.3	99.6	104.8	109.9	114.8	119.6	124.3	129.0	133.5	138.0	142.4
6	82.4	88.4	94.1	99.7	105.0	110.2	115.2	120.2	125.0	129.7	134.4	138.9	143.4	147.8
7	87.7	93.7	99.5	105.0	110.4	115.6	120.6	125.6	130.4	135.1	139.7	144.3	148.7	153.1
	TDN													
0	37.7	42.3	46.6	50.8	54.8	58.7	62.5	66.2	69.8	73.4	76.9	80.3	83.7	87.0
1	41.7	46.3	50.6	54.8	58.8	62.7	67.6	70.3	73.9	77.4	81.0	84.4	87.8	91.1
2	45.8	50.4	54.7	58.9	62.9	66.8	71.6	74.3	78.0	81.5	85.0	88.4	91.8	95.1
3	49.9	54.4	58.7	62.9	66.9	70.9	75.7	78.4	82.0	85.5	89.1	92.5	95.9	99.2
4	54.0	58.5	62.8	67.0	71.0	74.9	79.8	82.4	86.1	89.6	93.1	96.5	99.9	103.2
5	58.0	62.5	66.8	71.1	75.0	79.0	83.8	86.5	90.1	93.7	97.2	100.6	104.0	107.3
6	62.1	66.6	70.9	75.1	79.1	83.0	87.9	90.6	94.2	97.7	101.3	104.6	108.0	111.3
7	66.1	70.7	74.9	79.2	83.2	87.1	91.9	94.6	98.2	101.8	105.3	108.7	112.1	115.4

TABLE 23.4. *Continued*

B. In pounds, feed or *TDN*, per 100 fowls per day

No. eggs per week[26]	Body weight (lbs)												
	2.0	2.5	3.0	3.5	4.0	4.5	5.0	5.5	6.0	6.5	7.0	7.5	8.0
							Feed						
0	9.5	11.2	12.8	14.4	15.8	17.2	18.6	20.0	21.3	22.6	23.8	25.0	26.2
1	10.7	12.4	14.0	15.6	17.0	18.4	19.8	21.2	22.5	23.8	25.0	26.2	27.4
2	11.9	13.6	15.2	16.8	18.2	19.6	21.0	22.4	23.7	25.0	26.2	27.4	28.6
3	13.1	14.8	16.4	18.0	19.4	20.8	22.2	23.6	24.9	26.2	27.4	28.6	29.8
4	14.3	16.0	17.6	19.1	20.6	22.0	23.4	24.8	26.1	27.3	28.6	29.8	31.0
5	15.5	17.2	18.8	20.3	21.8	23.2	24.6	26.0	27.3	28.5	29.8	31.0	32.2
6	16.7	18.4	20.0	21.5	23.0	24.4	25.8	27.2	28.5	29.7	31.0	32.2	33.4
7	17.9	19.6	21.2	22.7	24.2	25.6	27.0	28.4	29.7	30.9	32.2	33.4	34.6
							TDN						
0	7.2	8.5	9.7	10.8	11.9	13.0	14.1	15.1	16.1	17.0	18.0	18.9	19.8
1	8.1	9.4	10.6	11.7	12.9	13.9	15.0	16.0	17.0	17.9	18.9	19.8	20.7
2	9.0	10.3	11.5	12.6	13.8	14.8	15.9	16.9	17.9	18.8	19.8	20.7	21.6
3	9.9	11.2	12.4	13.6	14.7	15.7	16.8	17.8	18.8	19.7	20.7	21.6	22.5
4	10.8	12.1	13.3	14.5	15.6	16.6	17.7	18.7	19.7	20.6	21.6	22.5	23.4
5	11.7	13.0	14.2	15.4	16.5	17.5	18.6	19.6	20.6	21.5	22.5	23.4	24.3
6	12.6	13.9	15.1	16.3	17.4	18.4	19.5	20.5	21.5	22.5	23.4	24.3	25.2
7	13.5	14.8	16.0	17.2	18.3	19.4	20.4	21.4	22.4	23.4	24.3	25.2	26.2

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[26] Assumed weight of egg 55 grams.

Data on the poultry and egg industry in the U. S. A.

Year	Millions on farm		Production billions per year			Consumption per capita per year			Cash farm income million $/year	
	Chickens	Turkeys	Chickens	Turkeys	Eggs	Chickens	Turkeys	Eggs	Poultry	Eggs
			lbs	lbs	no	lbs	lbs	no		
1930	469	6.0	2.6	0.23	43.0	21.6	1.8	331		
1936	404	5.7	2.5	0.41	38.0	19.0	2.7	289	317	485.1
1940	438	8.6	2.2	0.51	43.5	18.9	3.6	319	342	464.7
1941	423	7.3	2.6	0.53	45.9	20.3	3.6	316	448	658.0

Chapter 24

Energetic Efficiency of Muscular Work and Indices of Work-Reserve Capacity

> The horse raises what the farmer eats, and eats what the farmer raises. But you can't plow in the ground and get gasoline. You don't have to pay a finance company 10 or 15 per cent to own a horse. Brood mares work on the farm and raise colts as well. *Will Rogers*

24.1: Introduction. Agriculture has tended to follow the lead of industry in ever greater reliance on the free energy (Ch. 2) of petroleum and coal. The horse population has been declining,[1] the tractor population rising. There are several reasons for this trend in addition to the rapid progress in machine design. One is competitive overproduction of petroleum.

Petroleum fuels in most of Europe are too expensive for agricultural use, and America, too, is passing, or soon will be, from an economy of petroleum abundance to one of scarcity, perhaps reversing the present power trend in agriculture, in spite of the current hopes[2] for developing inexpensive petroleum-fuel substitutes.

Some countries, notably Germany, aware of the dwindling fuel oil, undertook to compensate in part by what is known in Europe as "work rationalization"[3] and in this country as "scientific management"[4] and "efficiency engineering." Systematic investigations have been organized on the physiology of work, especially in Germany. The Kaiser-Wilhelm Work Institute in Dortmund[5] (Fig. 24.22) was organized with this philosophy in mind. This institute is concerned with the physiology of work of man. An institute for the physiology of work of farm animals and farm laborers was being organized (at the time of the writer's visit to Germany in 1931) in Pommritz, near Breslau.[6] In Budapest, Farkas[7] and associates were investigating the physiology of work of farm laborers. Russia was organizing a number of work institutes,[8] as was Czechoslovakia.[9] While the energetics of work has been investigated in France since the time of Lavoisier, it was only by 1930, apparently following Germany's example, that a special work institute was organized in Paris.[10] An "Industrial Fatigue Board" has been organized in London.[11]

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[1] There are in the United States about 12 million working horses and mules and about 2 million colts. This is less than $\frac{2}{3}$ of the horse and mule population of 1920. The work-animal power is being replaced by petroleum-power machinery for which about a billion dollars was spent in 1937. While the replacement of horses by machines is rapid on the larger farms, yet perhaps $\frac{3}{4}$ of the U. S. farms—naturally, the smaller units—are operated by horse and mule power.

[2] There is no precedent for this hope, since with the exception of the relatively negligible hydroelectric developments, our dazzling material progress and discoveries have been based not on developments of renewable energy, but on exploitation of non-renewable "free energy" stored through the past ages. The use of alcohol, vegetable oils, peat and coal derivatives as fuels will be even more expensive in the future than they are at present. For other possibilities, see Ch. 25.

[3] Atzler, E., und Lehmann, G., "Rationelle Arbeit." Kaiser-Wilhelm Institut Für Arbeitsphysiologie, Dortmund, Hindenburgdam 301. Urwick, L., "The meaning of rationalization," London, 1929.

[4] Taylor, F. W., "The principles of scientific management," Harpers, 1919. Copley, F. B., "F. W. Taylor, Father of scientific management," Harpers, 1923.

[5] Atzler[3], The journal *Arbeitsphysiologie*, Berlin (Julius Springer); "Korper und Arbeit, Handbuch der Arbeitphysiologie," Leipzig (Thieme), 1927.

The interesting aspect of the "scientific management" or "efficiency engineering" movement, which originated in the United States, is that its physiologic aspects have been developed mostly in Europe. With the exception of the Harvard Fatigue Laboratory,[12] there is no institution in this country expressly devoted to the physiology and long-range efficiency of muscular work, certainly not of farm animals. It would seem that some provision should be made for research in this practically important and scientifically fascinating virgin field. Horses and mules are economical to the farmer in monetary cost and to the nation in "free energy" cost; they are especially desirable when ready cash is scarce and feed suitable for horses is plentiful, as is the case during our periodic depressions.

While it is theoretically easy to double or triple the average productive level of dairy cattle by merely utilizing available knowledge (Ch. 22), this cannot be said for improving the work capacity of horses because of lack of comparable knowledge for muscular work. We have learned to measure precisely milk production capacity but not work production capacity,[13] and we cannot improve a characteristic by breeding if we cannot measure it.

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[6] Derlitzki und Huxdorf, "Landarbeit wird erforscht," *Die Umschau*, **34,** 523 (1930). Huxdorf, *Fortschritte der Landwirtschaft*, **5,** 290 (1930).

[7] Farkas, *et al.*, *Arbeitsphysiol.*, **1,** 466 (1929); **3,** 468 (1930); **5,** 434, 549, 569 (1930).

[8] Simonson, E., *Klin. Wochenschr.*, **10** (1931).

[9] For the design of a Work Institute in Czechoslovakia see Institut pour l'économie du travail dans d'agriculture, près l'Académie Masaryk du Travail. IV. Congrès International l'organization scientifique du Travail, Paris, 1929. See also: Institute for the Economy of Labor, Prague High School of Agriculture and Forest Engineering at Uhrineves. 1930.

[10] Laboratoire de Physiologie du Travail. Conservatoire National des Arts et Métiers, 292 Saint-Martin, Paris. This laboratory published the journal *Le Travail humaine.*

[11] Typical publications: Cathcart, E. P., *et al.*, "The physique of women in industry, a contribution toward the determination of their optimal load." *Great Brit. Industrial Fatigue Board Pub.*, 44, 1927. Hill, L., *et al.*, "The kata-thermometer in studies of body heat and efficiency," Great Brit. Med. Res. Council, London, 1923. Vernon, H. M., *et al.*, "Rest phases in heavy work." *Med. Res. Council, Industrial Fatigue Bd.*, No. 41, 1927, and so on.

[12] For some work there accomplished see the following review by its director: Dill, D. B., "The economy of muscular exercise." *Physiol. Rev.*, **16,** 263 (1936). Dill, "Life, heat and altitude." Harvard University Press, 1938. Many papers by Dill are reviewed in this Chapter and in Chapters 11 and 6.

There is an obvious need for developing methods and their use for measuring quantitatively and precisely actual work performance and potential work capacity, and the influence of environmental and hereditary factors, including age, body size, sex, nutrition, climate, and so on. It is particularly desirable to develop potential work-aptitude tests in the animals when they are still young, analogous to the intelligence and other aptitude tests and quotients employed on children.

The following sections describe some contributions we have made[14] toward measuring work performance and capacity and their relation to the available knowledge in the literature.

Broadly speaking, muscular work may be divided into (1) thermodynamic and (2) physiologic aspects. The thermodynamic aspect is concerned mostly with energetic efficiency, previously discussed in outline (Chs. 1, 2, and 3) and here discussed in detail. Some physiologic aspects were likewise previously discussed, especially anaerobic oxidative metabolism in muscular work (Ch. 6), hormonal (Ch. 7), nutritional (Ch. 20), and temperature and humidity aspects (Ch. 11); oxygen transport as index of work capacity is here discussed for the first time.

24.2: Work performance and its energetic efficiency. *Work performed*, formally defined by the product of weight, W, by the distance pulled was measured with a treadmill actuated by a 5-horse power motor (Figs. 24.1, 24.2, 24.21). The rate of *energy expended* was measured by the rate of oxygen consumed.[15] In addition to the treadmill-closed-circuit metabolism apparatus illustrated in Fig. 24.21 used indoors, we also employ an ergometer-open-circuit apparatus used outdoors as illustrated in Fig. 24.23. This field apparatus consists of a weight ergometer modified after the Collins and Caine[22] ergometer, and an open-circuit apparatus for measuring and aliquoting the exhaled air, similar in principle to an earlier laboratory apparatus (see page 336). Fig. 24.23 shows how the ergometer is mounted on a trailer pulled by a motor car which also carries the open-circuit metabolism apparatus. The animal pulls a desired weight in the ergometer at the pace set by the car, just as on the treadmill (Figs. 24.1 and 24.21) the animal pulls desired weights at the pace set by the treadmill apron actuated by an electric motor.

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[13] Laughlin, H. H., *Sci. Monthly*, **38**, 210 (1934): "We have not learned to measure the physiological entity called racing capacity in horses." This is still more true as regards work capacity.

[14] Procter, R. C., Brody, S., Jones, M. M., and Chittenden, D. W., "Efficiency of work in horses of different ages and body weights." Univ. Mo. Agr. Exp. Sta. Res. Bull., 209, 1934. Brody, S., and Cunningham, R., "Comparison between efficiency of horse, man, and motor, with special reference to size and monetary economy." *Id.*, Res. Bull., 244, 1936. Brody, S., and Trowbridge, E. A., "Efficiency of horses, men, and motors," *Id.*, Res. Bull., 383, 1937. Kibler, H. H., and Brody, S., "An index of muscular work capacity." *Id.*, Res. Bull., 367, 1943.

[15] For details, see Chapter 12, where it is explained that the thermal value of oxygen ranges from 4.7 to 5.1 Cal per liter, but that it is convenient to assume that it is 4.825 Cal per liter.

The *unit of work* is the kilogram-meter; or the foot-pound, which is the work done by a force of 1 pound acting through a distance of 1 foot. Thus if a force of 1 pound is required to raise a window 1 foot, 1 foot-pound work is done in raising the window. A horse pulling on 150 pounds (as in Fig. 24.1) 2.5 miles (that is 13200 feet) accomplishes

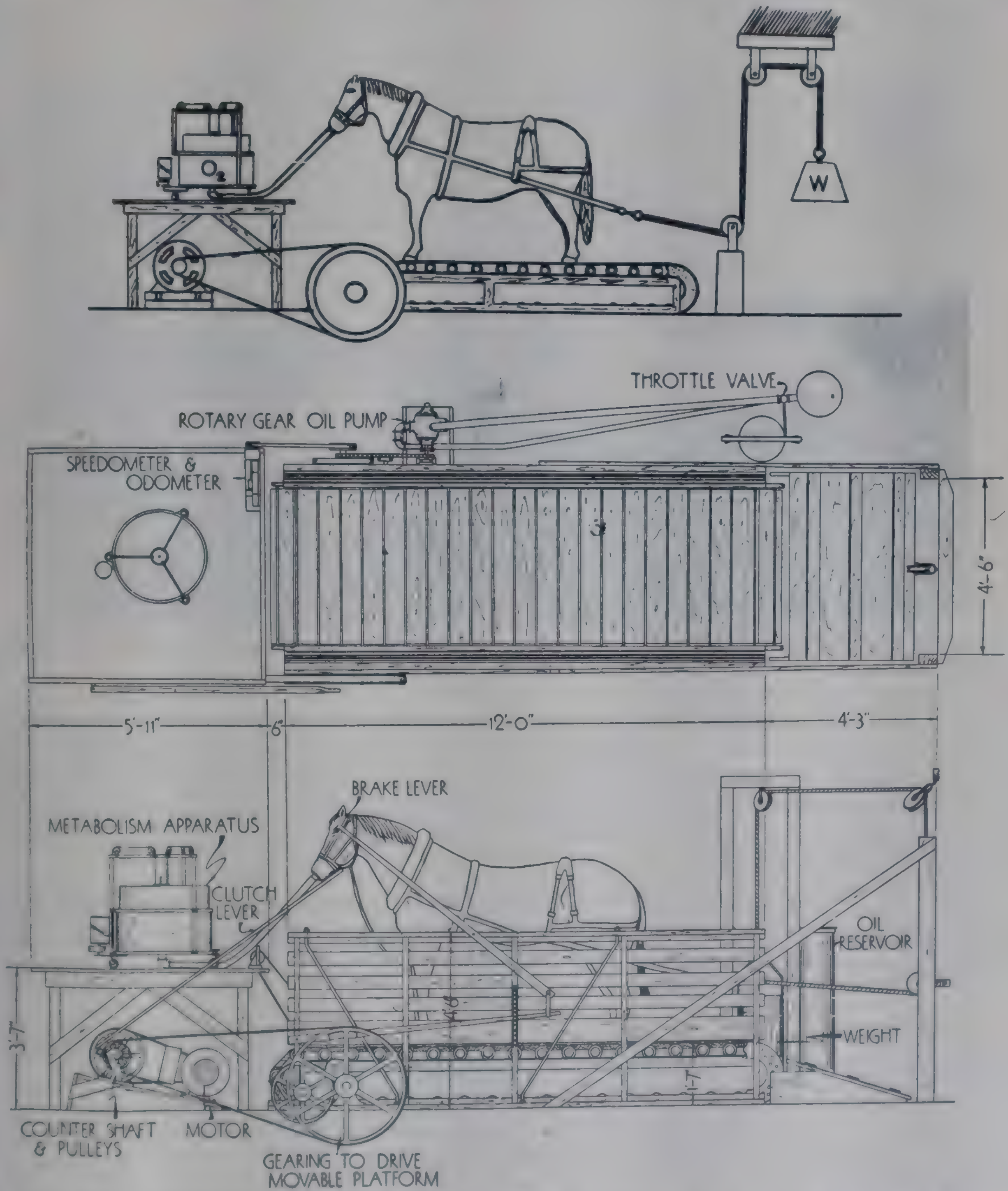

Fig. 24.1. Measuring work efficiency. Work consisted in pulling weight, W, on a moving horizontal platform actuated by an electric motor at desired speeds; energy cost was computed from the rate of oxygen consumption from tank O_2.

150 × 13200 = 1,980,000 foot-pounds, or 642 Calories of work. One ft-lb = 0.1382 Kg-meters = 0.005 ft-ton = 0.000324 Cal; or 1 Kg-m = 7.233 ft-lb = 0.002344 Cal; or 1 Cal = 426.4 Kg-m = 3087 ft-lb. (See Sect. 2.4 for other energetic equivalent values.)

Efficiency is the ratio of the Calorie equivalent of work energy performed to Calories expended. Thus a horse pulling 150 pounds (as in Fig. 24.1) 2.5 miles (that is 13,200 feet), accomplishes 150 × 13200 = 1,980,000 foot-pounds, equivalent to 640 Calories. If the horse consumed oxygen equivalent to 3210 Calories for performing this work, the energetic efficiency of the work is 642/3210 × 100 = 20 per cent.

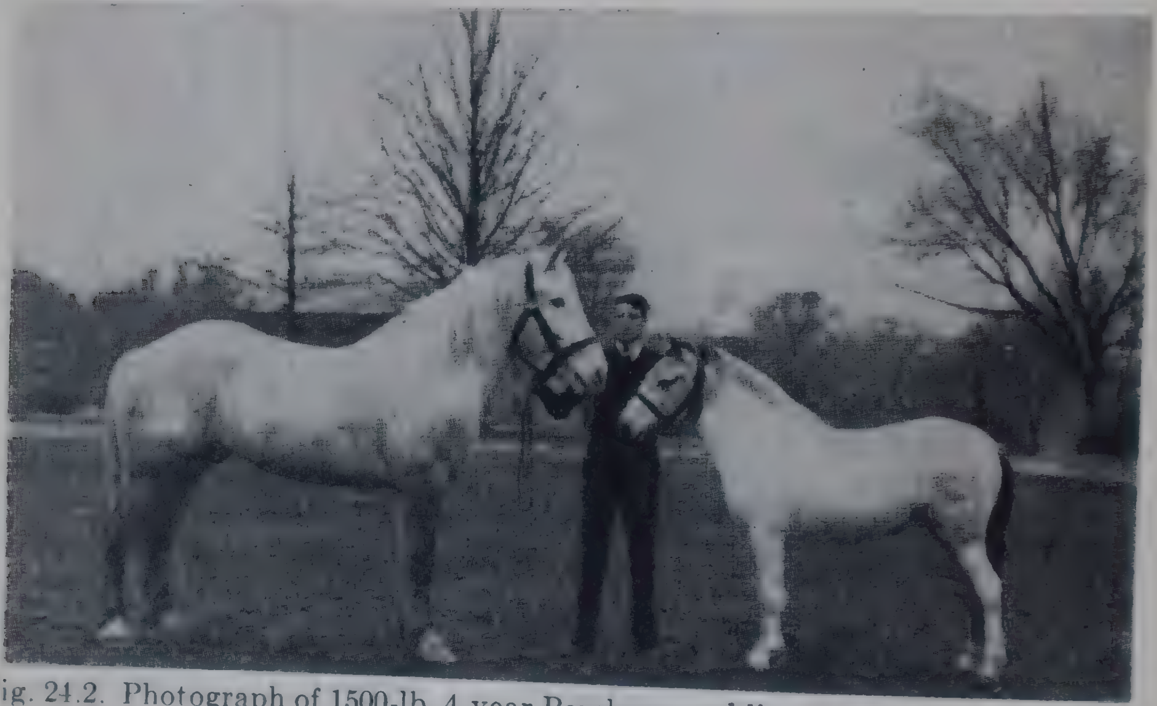

Fig. 24.2. Photograph of 1500-lb. 4-year Percheron gelding 19 and of 3-year old 600-lb. Shetland Pony 2 which furnished the bulk of the data.

Work rate (work *per unit time*) is measured in watts, kilowatts, or most commonly in this country in horse power. A horse power is work done at the rate of 1,980,000 foot-pounds per hour, or 33,000 foot-pounds per minute, or 4562.4 kg-meters per minute; or at the rate of 642 Calories per hour or 10.7 Calories per minute. A horse power is equivalent to approximately $\frac{3}{4}$ kilowatt or 746 watts, and a kilowatt is equivalent to approximately $1\frac{1}{3}$ horse power.

Work rate combines three factors into one: load, distance, time; or speed and load. For instance, a work rate of one horse power or 33,000 foot-pounds per minute is obtained when the animal pulls in 1 minute 1 pound for 33,000 feet, or 33,000 pounds for 1 foot. The product is, in both examples, 33,000.

As previously explained (eqs. in Ch. 3) we adopted three energetic efficiency categories: *gross*, *net*, and *absolute*, as defined by the equations:

$$\textit{Gross efficiency} = \frac{\text{work accomplished}}{\text{energy expended}} \tag{3.1}$$

$$\textit{Net efficiency} = \frac{\text{work accomplished}}{\text{energy expended above that at rest}} \tag{3.2}$$

$$\textit{Absolute efficiency} = \frac{\text{work accomplished}}{\text{energy expended above that of walking without the load}} \tag{3.3}$$

The energy expended (denominator) is in all cases measured by the rate of oxygen consumption, that is, by the rate of oxidation of the metabolites. The energetic efficiency of muscular work here discussed thus has a different significance than the energetic efficiency of milk production or egg production discussed in the preceding chapters. In the preceding chapters the efficiency is with reference to the nutrients (*TDN*) consumed by the animal; in this chapter it is with reference to the metabolites oxidized in the body as measured by the rate of oxygen consumption (Ch. 12). The energetic efficiency with reference to the oxidized metabolites is, of course, greater than it would be with reference to the energy of the consumed feed, because there is considerable waste in converting feed into body metabolites, and this waste, charged to the animal, would reduce the overall computed efficiency.

It is instructive to compare the energetic efficiency of various transformers. The following energetic-efficiency values are from Hill:[16]

Steam engines without condensers	7½%
Steam engines with condensers	9 to 19%
Gas engines	14 to 18%
Diesel engines	29 to 35%

Needham[17] quotes the following figures:

Locomotive steam engine, not over	15%
Gas engine with suction producer	25%
Diesel engine, best recorded efficiency with high maximum pressure	40%
"Electric accumulator"	70 to 74%

The overall or gross energetic efficiency of farm tractors used in the Middle West (United States) is for the ignition-type[18] about 19 per cent at the belt, or 13 per cent at the draw-bar;[19] for Diesel type,[18] 26 per cent at the belt or 22 per cent at the draw-bar.

As explained before (eq. 2.5) the energetic efficiency of a slow-charging or discharging cadmium standard cell (an isothermal, or constant-temperature, process) is nearly 100 per cent; but the maximum energetic efficiency of the heat engine (which operates by virtue of temperature gradient) is, *at the usual emperature*, about 50 per cent for the theoretical Carnot engine and very much below this for actual engines as quoted above from Hill and Needham.

[16] Hill, A. V., "Muscular movements in man."

[17] Needham, J., "Chemical embryology."

[18] The ignition type engine has an electrical ignition system and burns refined fuels, such as gasoline; the Diesel type engine does not have an ignition system, the heat of compression ignites the fuel of a lower grade, such as fuel oil.

[19] In the "belt test," the tractor serves as a stationary engine supplying power to rotating machinery through the power take-off and a belt drive. In the "draw-bar" test the tractor pulls a known load, as measured by the draw-bar pull and the speed. The draw-bar efficiency is naturally lower because the tractor expends energy pulling itself over the ground.

Animals are, of course, not heat engines (Chs. 2 and 3) but isothermal converters, yet their maximal energetic efficiency is close to that of heat engines: about 25 per cent for *gross* efficiency (eq. 3.1), 28 per cent for *net* efficiency (eq. 3.2) and 35 per cent for *absolute* efficiency (eq. 3.3). The efficiency of the modern Diesel engine is about 40 per cent.

As before explained (Ch. 3), just as the theoretically (thermodynamically, Ch. 2) maximal efficiency of the Carnot engine is only about 50 per cent, so, according to Hill,[20] the theoretically maximum efficiency of a contracting muscle (an isolated frog-muscle strip) is approximately 40 per cent. Hill's theoretic efficiency is analogous to our absolute efficiency (eq. 3.3).

Assuming a theoretic 40 per cent efficiency of muscular work, what becomes of the remaining 60 per cent of the energy? Some is expended for overcoming external resistance (wind, contact of feet with ground, etc.); some is expended for useless incidental motions associated with work, and so on. Most of the energy is, however, expended for overcoming the internal resistance, the resistance of the body colloids. This internal resistance is energetically wasteful but biologically useful because without it the animal would "tear his tendons, break his bones, 'pull' his muscles, strain his joints".[20]

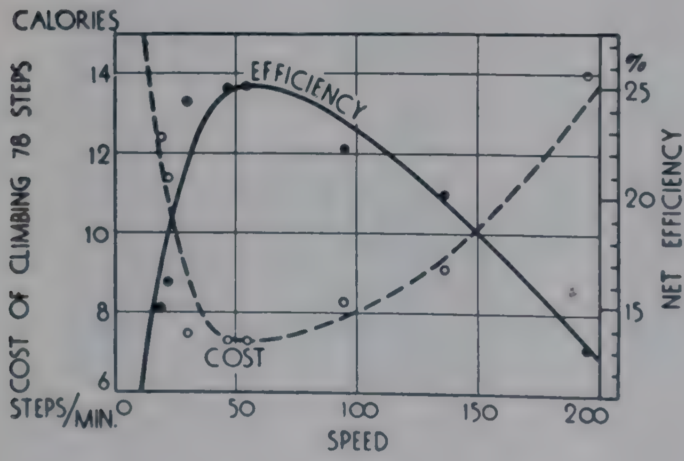

Fig. 24.3. Rise and decline of the net efficiency (not including maintenance, eq. 3.2) of climbing 78 steps with increasing climbing speed. From data by H. Lupton, *J. Physiol.*, **57,** 337 (1923).

A distinguishing characteristic of animals is that they expend energy even when not performing external work because the internal work—the maintenance cost—goes on regardless of external activity. Hence the all-day energetic efficiency of animals varies with the number of hours worked (Fig. 24.10a to 24.10c).

Then, too, the slower the speed of work, the longer the time taken for holding the muscles in a state of unproductive tension, that is, the greater the maintenance cost per unit work. On the other hand, the greater the speed of work the greater the energy cost in overcoming internal resistance to the muscular contractions of the viscous colloids which make up the body. The efficiency of muscular work as function of speed may, therefore, be expected to be of a rising and declining type[21] (Fig. 24.3), resembling the rising and declining course of efficiency as function of speed in the automobile (Fig. 24.4).

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[20] Hill[16] and Ch. 3.

We have not observed such a rising and declining curve for farm work horses pulling loads at speeds ranging from 1.15 to 3.1 miles per hour as graphed in Fig. 24.5a and b. The highest walking speed was too low to bring

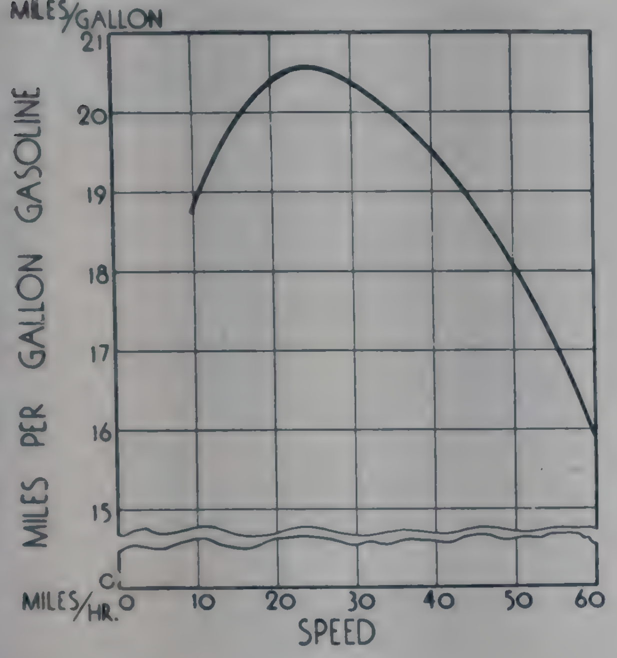

Fig. 24.4. Influence of speed of driving a car on efficiency in terms of miles travelled per gallon gasoline.

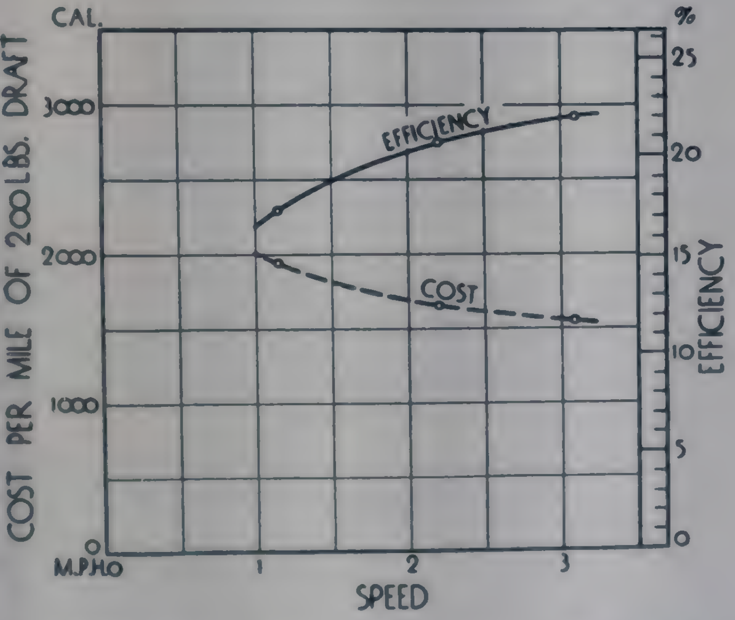

Fig. 24.5a. Influence of 3 working speeds on gross work efficiency of horse 19 pulling 300 lbs.

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[21] Efficiency of climbing 78 steps. Plotted from data by Lupton, H., *J. Physiol.*, **57**, 337 (1923). Benedict and Murschhouser, H., Carnegie Inst. Publ., 231, 1915, likewise found an optimum speed for walking as shown by the following table:

Meters walked per minute	53	60	80	90	102	140	146
Calories expended per min	64	58	52	51	53	73	77

See also Benedict and Parmenter, *Am. J. Physiol.*, **84**, 675 (1928), and Benedict and Cathcart, Carnegie Inst. Wash. Publ., 187, 1913.

out the declining phase of the curve. Attempts to increase the rate of walking beyond 3.1 m.p.h. for 1500-lb horse 19, or 2.2 m.p.h. for 700-lb pony 2, changed the walking into trotting, which we wished to avoid, partly because under working conditions loads are pulled by walking rather than trotting, and partly because of the danger to horse and treadmill in case of breakdown.

The highest rate of work at the walking speed of horses may be too low to bring out the efficiency-depressing effect of the internal friction observed at higher speeds of movement. In such case it would appear that the higher the rate of work the higher would be the *immediate* energetic efficiency of work (Fig. 24.5a). The maximum *long-range* or life-time efficiency, however, involves liberal rest periods and moderate work rate. One of the problems of "scientific management" or "work rationalization," whether it be of man, cow, or horse, is to determine for animals of given productive capacity the work level for maximal long-range efficiency.

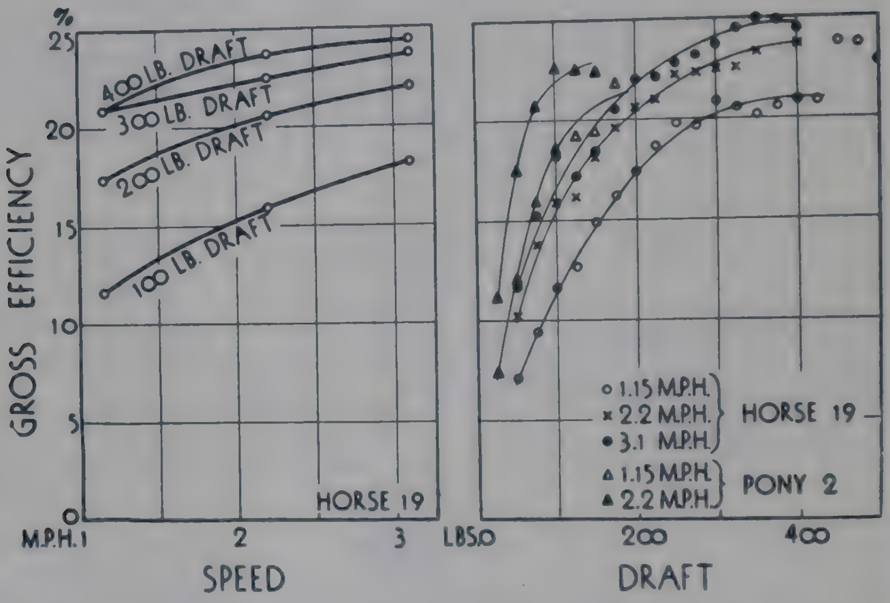

Fig. 24.5b. Influence of pulling speed for given loads, and of load for given speeds on gross efficiency. Gross energetic efficiency rises with increasing speed and load (between the given limits), but the rises are at decreasing increments.

Machines are not usually run at more than 50 per cent of their capacity, and a similar safety margin should perhaps be allowed to man and animals so as to avoid injury or untimely death. The problem in work rationalization is to determine the maximum rate of work that can be carried on day in and day out and still retain vigor to an advanced age. A tentative recommendation for the average horse in Missouri is a tractive draft equal to 10 per cent of body weight pulled at about $2\frac{1}{2}$ miles an hour.[22] This will usually amount to work at the rate of about 4 kilowatts or 1 horse power (33,000 foot-pounds or 10.7 Cal per minute).

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[22] Collins, E. V., and Caine, A. B., Iowa A. E. Sta. Bull., 240, 1926, reported that it is possible for horses weighing 1500 to 1900 lbs. to work continuously (10 hrs. a day) at a rate of 1 horse power; or that it is possible to exert a tractive effort of 1/10 of their body weights and travel a total of 20 miles per day without damaging fatigue.

Fig. 24.6a shows that while horses can pull loads at least up to 35 per cent of body weight, increases in efficiency become negligible after the draft exceeds 15 per cent of body weight: the rise in energetic efficiency with increasing work rate follows the law of diminishing returns (Ch. 1). When horse 19 works at ½ horse power, his efficiency is 12½ per cent; doubling the work rate to 1 horse

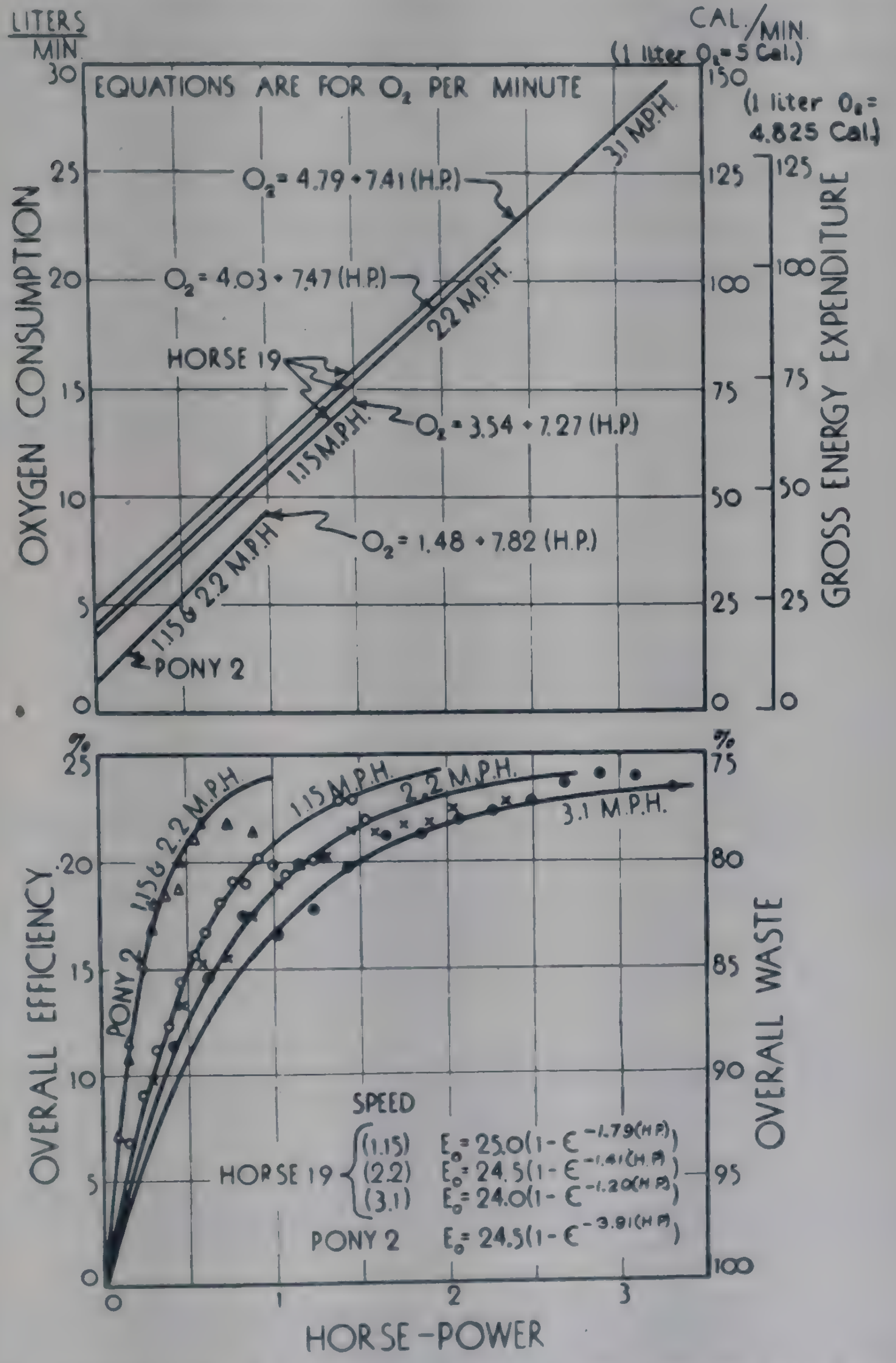

Fig. 24.6a. Gross or overall efficiency and oxygen consumption plotted against horse-power. The oxygen consumption or energy expense increases directly (linearly) with increasing rate of work; the efficiency, however, increases at decreasing increments (exponentially) with increasing rate of work. For a given horse power the oxygen consumption per unit time decreases, and overall efficiency increases with decreasing speed.

power does not double his efficiency to $12\frac{1}{2} \times 2$, or 25 per cent, but only to 18 per cent; at 2 horse-power, his efficiency is not $12\frac{1}{2} \times 4$, or 50 per cent, but only 22 per cent; at 3 horse power his efficiency is not $12\frac{1}{2} \times 6$ or 75 per cent, but only 24 per cent. In other words, the efficiency lags increasingly behind the increase in work rate. Hence the work rate should not increase beyond the point at which the curve begins to flatten decidedly, beyond about 1 horse power, which is the customary rate of work for the 1600-lb horse.

Within the speed limits investigated—that is, 1.1, 2.2, and 3.1 miles per hour—the slower the speed (with a compensatingly higher load) for a given horse power the greater the energetic efficiency of the work. Thus at a working rate of 1 horse power, the efficiencies for horse 19 were: 17 per cent for 3.1 miles per hour; 19 per cent for 2.2 m.p.h.; 21 per cent for 1.15 m.p.h.

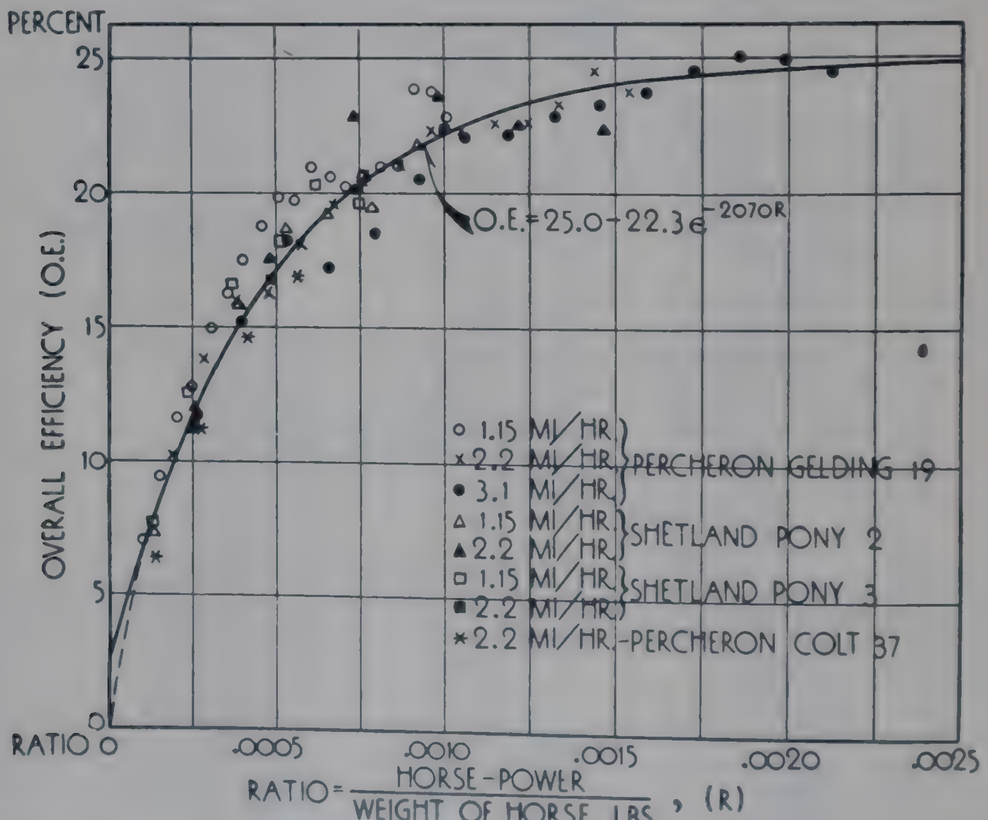

Fig. 24.6b. The curves in the lower half of Fig. 24.6a coincide if plotted against the ratio of H. P. to body weight.

Hence from the standpoint of highest energetic efficiency, work horses are more efficient *working at a given horse power* at a slow speed pulling a heavy load than at a high speed pulling a light load, perhaps because the energy losses of overcoming the colloidal resistance of the muscles increase more rapidly than the speed of walking. However, the total energy cost for accomplishing a given job is less at a higher speed because of the saving of maintenance expense resulting from the reduction in the time required to complete the job (provided that the increased time required for recuperation following work at a higher speed is not included in the expense).

Fig. 24.6b shows that if overall or gross efficiency of muscular work is plotted against the ratio of the rate of work (horse power) to body weight, the data for all animals and speeds fall on the same exponential curve

$$E = A - Be^{-kR}$$

in which E is gross energetic efficiency at the ratio, R, of horse power to body weight. The increase in efficiency occurs at diminishing increments, exponentially (Chs. 5 and 16).

If, however, the gross efficiency is plotted against horse power (rather than against the ratio of horse power to body weight) each speed and each animal yields an exponential working curve different from the other curves.

While the graph of *efficiency* as function of work rate is exponential, that of absolute *energy expense* against work rate is linear. The equations, given on the charts,[23] show that the limiting or maximal gross energetic efficiency of muscular work in horses is 25 per cent, and that this maximum is approached exponentially. At the upper limit of our work schedule our larger horses (1500–1600 lb) are seen to have consumed oxygen at the rate of 30 liters a minute, equivalent to an energy expenditure of 150 Calories a minute, which, as will be presently shown by Dill's result, is six times the maximal oxygen consumption in 150-lb man.

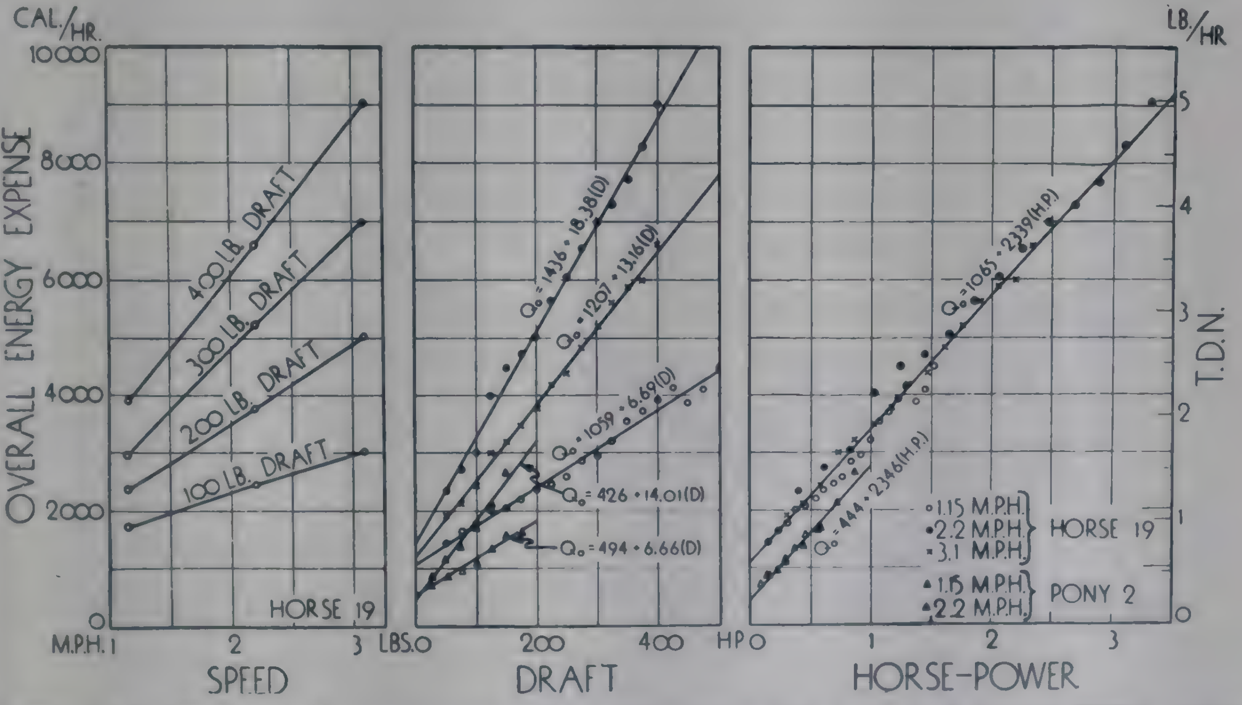

Fig. 24.7. The rate of energy expenditure (Calories, left axis, and pounds TDN, right axis) increases directly (linearly) with increasing speed, draft, and horse-power.

Fig. 24.7 shows the influence of speed, draft (load), and horse power on the rate of energy expenditure. At the upper limit of our work schedule our largest horse expended energy at the rate of about 9000 Cal/hr, equivalent to about 5 lb TDN/hr.

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[23] For detailed mathematical properties of these curves see Univ. Mo. Agr. Exp. Sta. Res. Bull., 244.

In computing the three categories of efficiency, gross, net, and absolute (eq. 3.1 to 3.3), it was necessary to measure the energy costs of standing and of walking.

The energy cost of standing above lying is about 9 per cent in man,[24] cattle and sheep.[25] One unusually heavy steer had a 13 per cent heat increment of standing above lying.[25] The ventilation rate was increased by the same percentage but the pulse rate[25] increased only 3 per cent. Horses are unique in not having a heat increment of standing; they do not spend more energy during standing at maturity[26] or during growth.[27] This is because horses have unusually powerful suspensory and check ligaments, and horses appear to rest and indeed sleep as comfortably while standing as while lying.

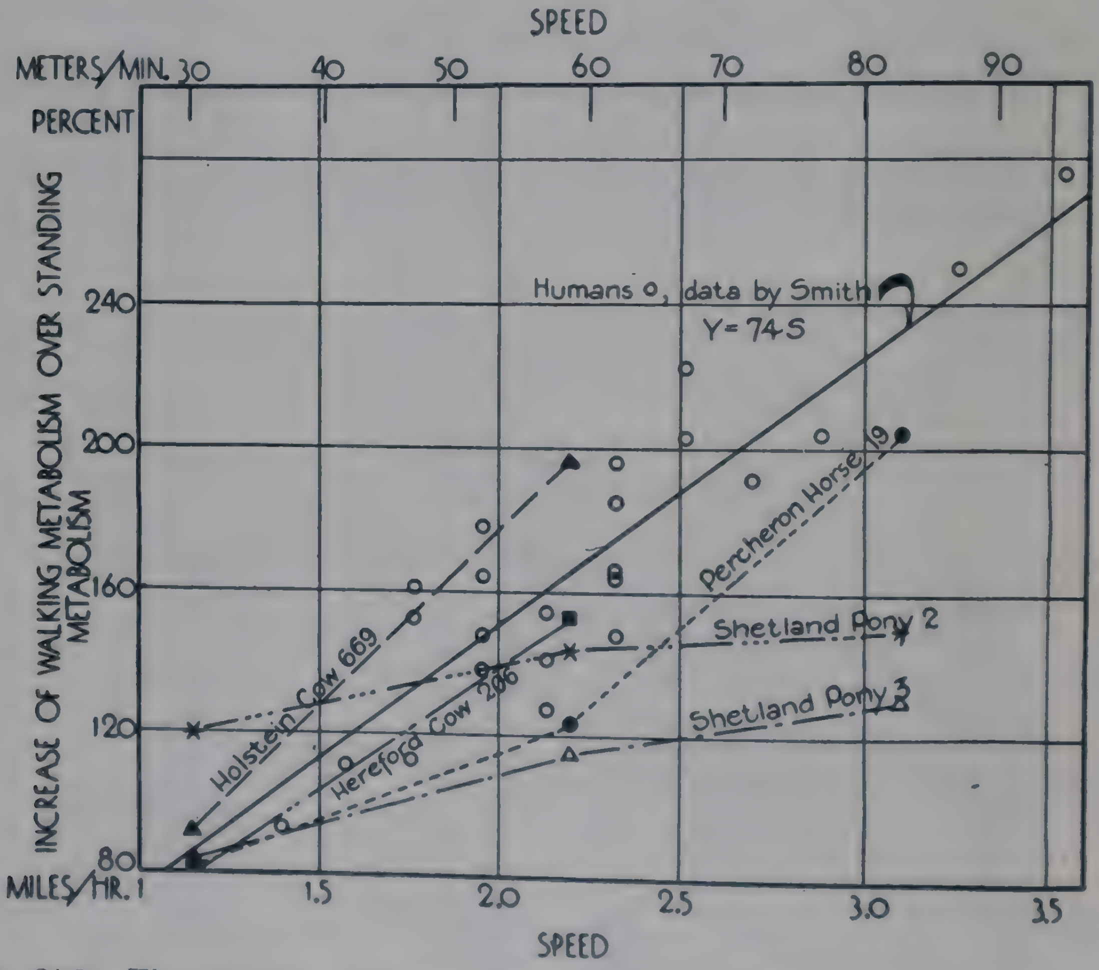

Fig. 24.8a. The percentage increase of walking over standing metabolism as function of speed. The light circles represent Smith's data on humans to which we have fitted (by method of least squares) the equation. The other data are original.

Walking consists in successive lifting of the body and the energy cost of walking should vary with the weight of the animal and the speed of walking.

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[24] Benedict, F. G., and Johnson, A., *Am. Phil. Soc.*, **58**, 89 (1919).
[25] Hall, W. C., and Brody, S., Univ. Mo. Agr. Exp. Sta. Res. Bull., 180, 1933.
[26] Winchester, C. F., *Science*, **97**, 24 (1943).
[27] Brody, S., and Kibler, H. H., Univ. Mo. Agr. Exp. Sta. Res. Bull., 368, 1943.

We investigated[28] 7 horses ranging in weight from 200 to 1500 lb (91 to 688 Kg); 7 cattle, 850 to 2000 lb (383 to 930 Kg); and 2 men, 70 to 75 Kg with results graphed in Fig. 24.8a. For purposes of comparison we also graphed Smith's data[29] on walking in man. Fig. 24.8a shows that *in man* the *percentage* increase in heat production during walking over standing varies

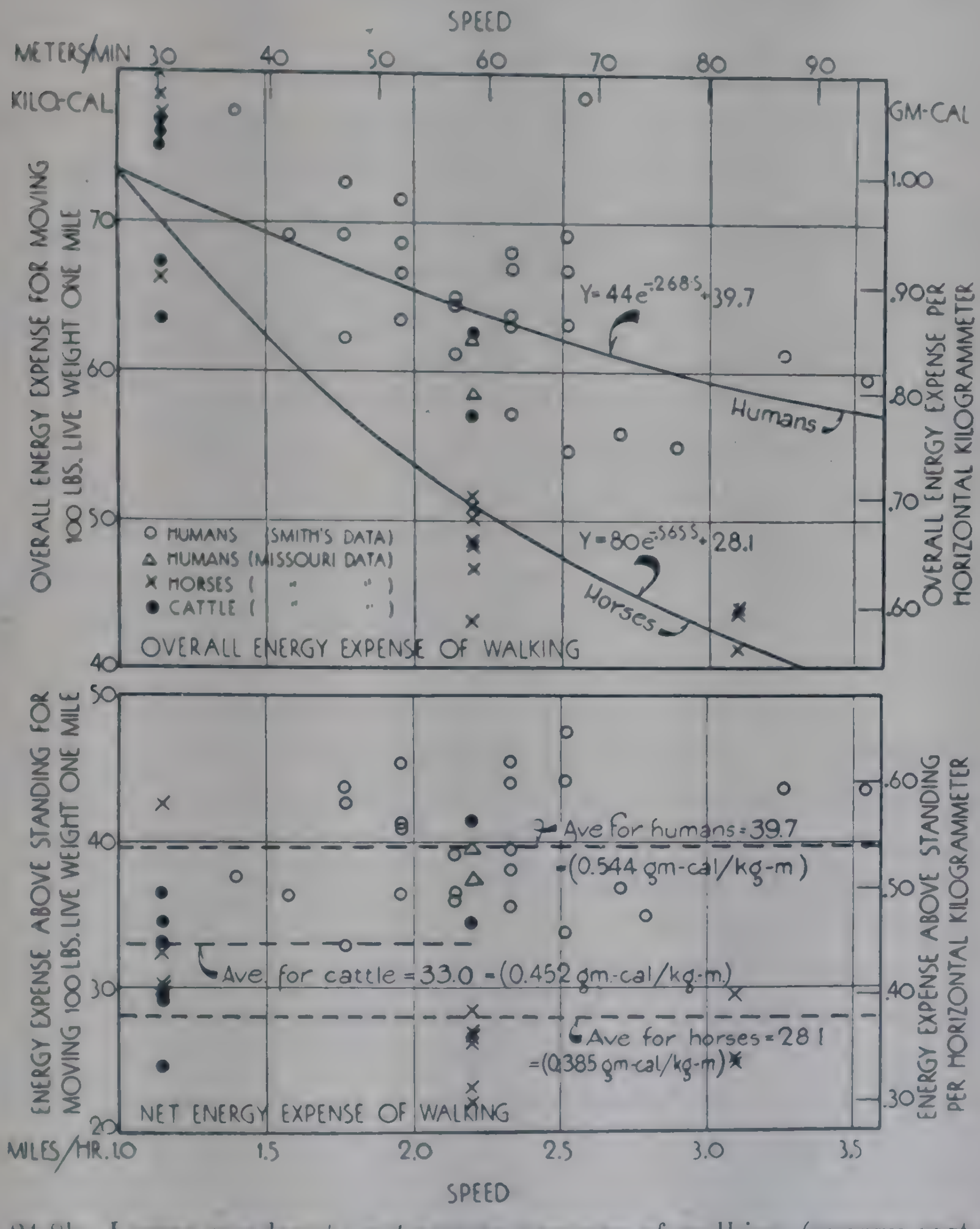

Fig. 24.8b. Lower quadrant: *net* energy expense of walking (energy cost of walking, not including the energy cost of standing); upper quadrant: *overall* energy expense of walking (including the cost of standing). Values are in terms of Calories per unit live weight and unit distance walked (metric units on top and right; English units on bottom and left side).

directly with the speed, given by the equation $Y = 74S$, in which Y is the percentage increase in heat production and S is speed of walking in miles per hour. At one mile per hour, the heat production is 74 per cent above standing; at two miles per hour, it is 148 per cent above standing, and so on. The percentage increase in cattle is of the same order as in man, but in horses it is less than in man.

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[28] Hall, W. C., and Brody, S., *Id.*, Res. Bull., 208 (1934).
[29] Smith, H. M., Carnegie Inst. Wash. Publ., 309, 1922.

As regards the caloric cost of walking, the upper chart in Fig. 24.8b shows that the overall cost (including the rest-maintenance component) per unit live weight decreases with increasing speed approaching 39.7 Calories per 100 lb. per mile as limit, as indicated by the equation

$$Y = 44e^{-0.268S} + 39.7$$

in which Y is Cal/100 lb wt/mile, and S is speed of walking. The higher the speed the less the overhead charge per unit ground covered and, therefore, the less the overall cost. If, however, the rest-maintenance item is not included in the total cost, the cost of walking is independent of speed. In terms of Calories per 100 lb live weight this *net*[30] energy of walking one mile is, in round numbers, 40 for humans, 33 for cattle, and 28 for horses. (In terms of gm-cal per kg-m it is 0.544 for humans, 0.452 for cattle, and 0.385 for horses.) These values (per unit live weight and per unit horizontal distance walked) are apparently independent of live weight for a given species and given state of fatness. Horses spend less energy moving unit body weight per unit horizontal distance than humans or cows. Cows and humans spend almost the same amounts of energy per unit live weight and unit distance. Fasting decreased metabolism both during standing and walking, but the percentage increase due to walking tended to increase with increasing time after feeding.

Summarizing, this section defines the units of work, rate of work, and energetic efficiency and presents methods for measuring them. Extensive data and generalizations (equations) are presented on the absolute and relative energy costs of standing, walking at various speeds, and working at various rates by varying load and speed. The immediate and long-range energetic efficiencies of various categories of work machines were compared critically.

24.3: Relative metabolism in steady, maximum, and brief peak effort. The rate of oxygen consumption or heat production is, of course, a function, among other factors, of body weight and work rate. The statement that an animal consumes oxygen at the rate, for example, of $\frac{1}{4}$ liter/min or produces heat at the rate of 1.2 Cal/min is, therefore, ambiguous unless given with reference to some standard size and work rate. In this section we shall take the resting oxygen consumption (approximately $\frac{1}{4}$ liter/min for adult male man) as reference base and express other values as multiples of this reference base. In the preceding section it was shown that the energy cost of walking is about 100 per cent above that of standing; that the ratio energy expense of walking/energy expense of standing = 2, and that this ratio is approximately the same in relatively large and small animals, horses, cattle, sheep, men. In this section we shall consider similar ratios for various work levels.

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[30] The net energy cost of walking does not include the energy cost of standing at rest, while the overall or total energy cost does.

24.3.1: Ratio of maximum to minimum oxygen consumption in horses and men. Fig. 24.9a shows ratios of maximum to minimum oxygen consumption in horses plotted against speed, load or draft, and horse power. The ratios of work oxygen to *resting* (not basal) oxygen increase to about 15, while the ratios of work oxygen to *basal*-metabolism oxygen increase to about 21. Since the top values represent work near the maximum of the animal's ability under the given conditions, it is concluded that the maximum amount of oxygen that

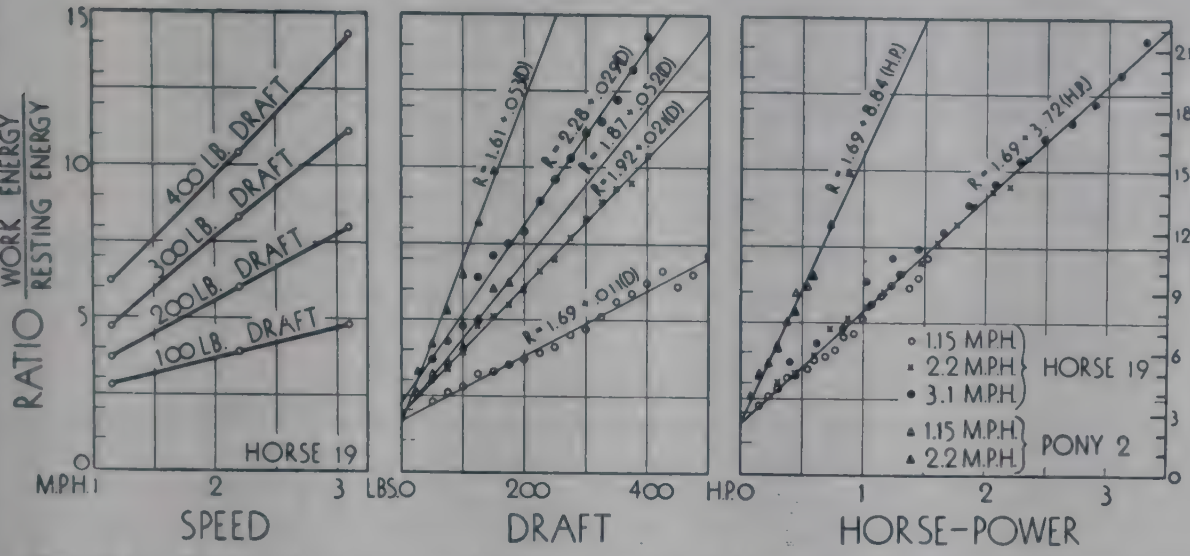

Fig. 24.9a. Ratio of work to rest oxygen on left side, and ratio of work to basal oxygen on right side plotted against speed, load, and work rate (horse-power). These ratios do not include possible "oxygen debt", therefore, they are not peak-efforts of which animals are capable (including oxygen debt), but ratios of maximum to minimum oxygen consumption.

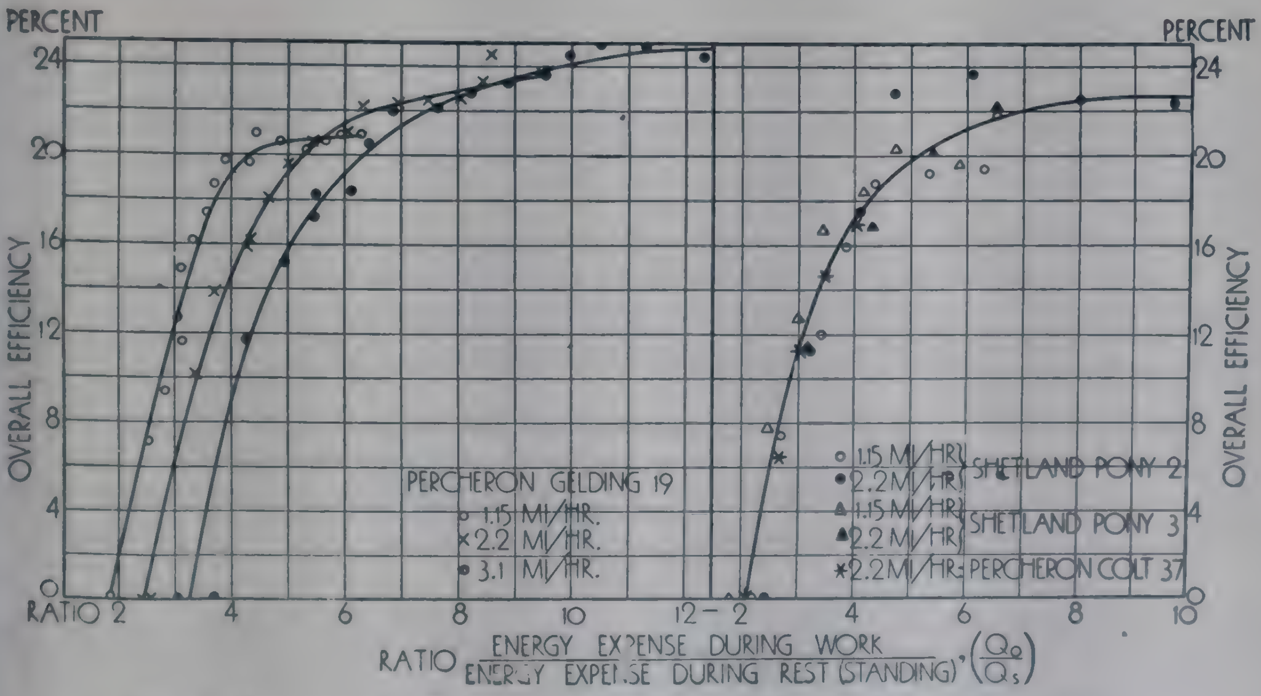

Fig. 24.9b. Overall efficiency as function of the work to rest energy.

a work horse can utilize is about 21 times the minimum or basal oxygen.[31]

According to Dill[32] the ratio of maximum oxygen consumption by men running at top speed to basal oxygen consumption varies from 10 to 20, depending on physical development and training. We, therefore, conclude that our 1500-pound work horse in excellent physical condition had approximately the same ratio of maximum to minimum oxygen consumption as a man in excellent condition. The ratio of work to resting oxygen consumption is apparently independent of size or even species; which means that in comparison to body weight, the limiting system concerned with supplying the muscles with oxygen is of the same relative capacity in superior work-horses as in superior athletic men. Race horses of extraordinary physical development and training probably have higher ratios than men or work horses. This is an attractive problem for study.

Data by Sargent[33] indicate that the maximal oxygen intake was 15-fold resting in a 63-kilo athlete. Schneider and Clark[34] reported (on R. W. C.) a 10-fold oxygen consumption when working a bicycle ergometer 8000 foot-pounds per minute (2.66 liters oxygen per minute) than at *rest* (0.282 liters per minute). Hill's tabulation[35] shows that a 184-pound oarsman (H) consumed 4.41 liters oxygen per minute; 147-pound runner (S) consumed 4.38 liters oxygen per minute. These oxygen consumptions correspond roughly to 1323 and 1314 Cal per hour. Assuming basal metabolism levels of 76 and 65 Cal per hour, the ratios of maximum to basal energy are 17 and 20, thus substantiating Dill's conclusion that the oxygen supply to the tissues is limited to about 20 times basal metabolism.

More recently Dill[36] observed a famous 2-miler, Lash, consume 5.35 liters oxygen, 21.4 times the basal level (of $\frac{1}{4}$ liter O_2/min), when running at the rate of 21.6 km/h, approximately the pace that he runs in his 2-mile winning races. This is said to be the highest oxygen-consumption record,[37] and contrasts to 14.5 times the basal level of oxygen consumption in the best untrained controls. This high rate of oxygen consumption is attributed to the extremely high cardiac output since the oxygen-carrying capacity of the blood was virtually the same as in the non-athletes. Incidentally, the highest pulse rate was 189 and the blood lactic acid 73 mgm per cent. At a lower work rate, 11.3 km/h on an 8.6 per cent grade, the athlete's pulse rate rose to 171 and the non-athletes' to 190.

The ratio of the work to resting oxygen consumption may be used for estimating physiological work-equivalence in different animals. Thus from Fig. 24.9a, when the ratio work O_2/basal metabolism O_2 is 10, work in the Shetland pony at the rate of 0.6 H.P. is equivalent to work in the Percheron horse at the rate of 1.4 H.P., and so on.

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[31] In preparing Fig. 24.9 it was assumed that the basal metabolism of the 1500-lb. horse is 400 Cal per hour (see Table 13.7); the standing metabolism, including the normal heat increment of feeding, 606 Cal/hr.

[32] Dill, D. B., *Physiol. Rev.*, **16**, 263 (1936).

[33] Sargent, R. M., *Proc. Roy. Soc.*, **100B**, 10 (1926–7).

[34] Schneider, E. C., and Clark, R. W., *Am. J. Physiol.*, **74**, 334 (1925).

[35] Hill.[16]

[36] Robinson, S., Edwards, H. T., and Dill, D. B., *Science*, **85**, 409 (1937).

[37] For other high records, see Henderson, Y., and Haggard, H. W., *Am. J. Physiol.*, **12**, 264 (1925); Christensen, E. H., *Arbeitsphysiol.*, **5**, 463 (1931).

24.3.2: Ratio of maximum effort, including the oxygen debt, to rest energy in men and horses. The preceding discussion was concerned not with peak-effort *energy expenditure*, but with peak-effort *oxygen-consumption*. The maximum energy expenditure is very much greater than the corresponding maximum oxygen consumption because (Sect. 6.2), animals (unlike engines) go into *oxygen debt* in emergencies and repay it later during rest. Athletes have been known to incur an oxygen debt of 8 liters during 15 seconds of sprinting at top speed. Such intense anaerobic efforts can last only a few seconds but are of tremendous value in emergencies. The ability to go into oxygen debt varies; great athletes usually have exceptionally high abilities in this direction. Superior race horses may be able to incur a greater oxygen debt than inferior ones. How does peak-effort energy to basal energy in man differ from that in the work horse?

The following table, based on the 1925 Iowa State Fair horse-pulling contest, indicates the order of peak effort in the winning heavy-weight teams.[38]

Trial	Distance pulled (feet)	Duration of trial (seconds)	Tractive pull (pounds)	Horse-power
1	27½	4.0	2000	25.0
2	27½	4.2	2500	29.8
3	27½	11.0	3000	13.6
4	27½	8.0	3200	20.0
5	27½	11.0	3400	15.5
6	27½	9.8	3425	17.5

Since the teams were made up of two horses, the rates of energy expenditure per horse are half the above values, 7 to 13 H.P. This table shows, then, that a 1500-pound horse can develop 7 to 13 H.P. during about 5 seconds. Assuming that the energetic efficiency of the pull is 20 per cent, the horses expended energy at the rate of 35 to 65 H.P. or (since 1 H.P. is equivalent to 10.7 Cal/min) 375 to 803 Cal/min. Since the basal metabolism energy of a 1500-pound horse is about 7 Cal/min, the ratio of peak energy expenditure to basal metabolism energy in the horse is 375/7 to 803/7 = 53 to 115. In brief, *a work horse is capable of spending about 100 times as much energy at maximal effort (for a few seconds) as during rest.*

As previously noted (Sect. 6.2) Fenn reported that a medical student performed at the rate of 139 Cal/min. If his basal metabolism was 1.2 Cal/min, the ratio of peak energy expenditure to basal energy was 139/1.2 = 116.

24.3.3: Ratio of sustained hard work to rest energy in men and horses. According to Dill,[32] the ratio of sustained-work energy (as is carried on in the usual 8–10 hour day) to basal-metabolism energy ranges in man from 3 to 8 in hard work (lumbering, building, mining, agriculture) to less than 3 for moderate work. How do these ratios for humans compare to those in horses?

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[38] Collins and Caine.[22]

As previously noted, a good pace for a 1500-lb. farm horse is work at the rate of 1 H.P. From Fig. 24.9a, the work to basal-metabolism energy ratio for a 1500-lb horse working at the rate of 1 H.P. is of the order of 8, which is the same as that given by Dill for human labor at hard work. Hence, the conclusion that the ratio of sustained hard work to rest energy is approximately the same in horse and man, and probably independent of size or even of species as such. Note from Fig. 24.9b how the overall efficiency for Horse 19 flattens sharply when the work-to-rest ratio is between 5 and 8.

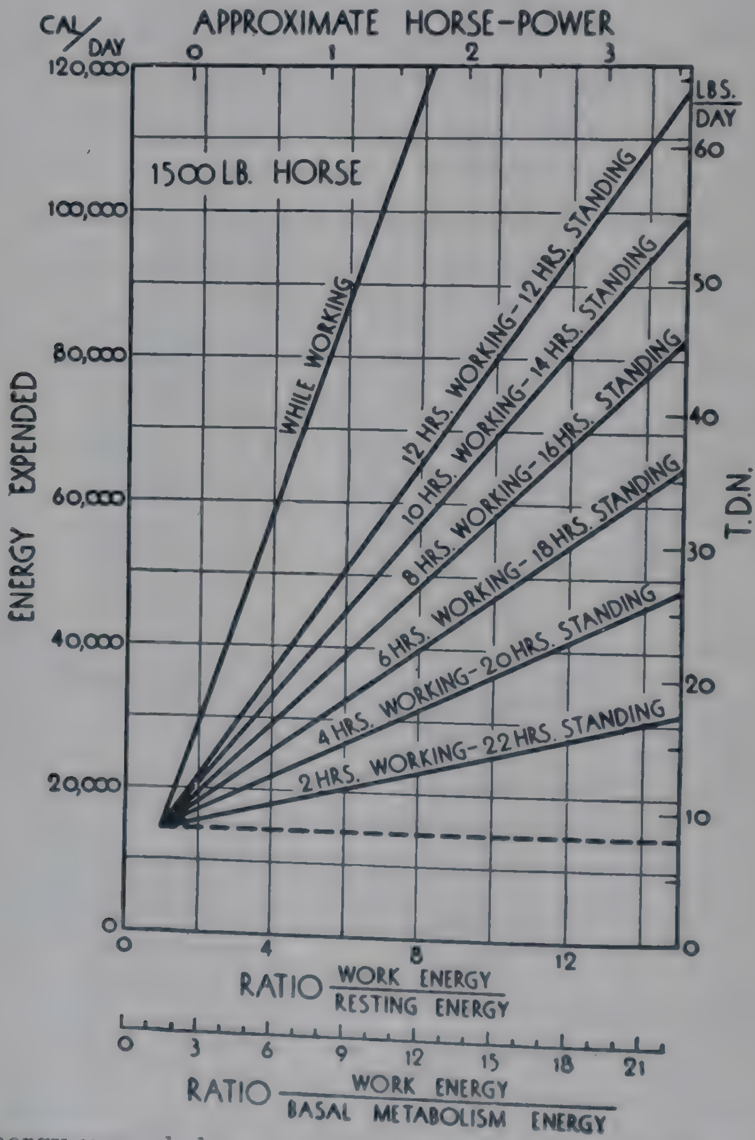

Fig. 24.10a. Energy expended per day (24 hours) plotted against ratios of work energy to: basal energy and to non basal resting energy when the horse works 0, 2, 4, 6, 8 10, 12, and 24 hours per day, and stands the remainder of the time.

The energy expended per 24-hour day, including the resting periods, is for humans from about 3000 Calories for moderate work to 6000 Calories for hard work (when the work to rest energy is near 8); that is, from 1.3 to 4 times the basal energy. It is instructive to know how the 24-hour energy expenditure in horses varies with the number of hours worked when working at different rates. From Fig. 24.10a, when the 1500-lb horse works 8 hours a day at a work-to-basal metabolism ratio of 8, he performs at the rate of about 1 H.P., and expends energy at the rate of 38,000 Calories per 24-hour day, corresponding to 21-lb TDN. At this rate of work the 1500-lb horse expends 38000/6000 = 6 to 7 times as much energy as a 150-lb man; which is what might be expected on the basis of the assumption that average work rate and energy expense vary with $W^{0.73}$. Similar curves are given in Fig. 24.10b for horses working 2, 4, 6, 10, and 12 out of the whole 24 hours.

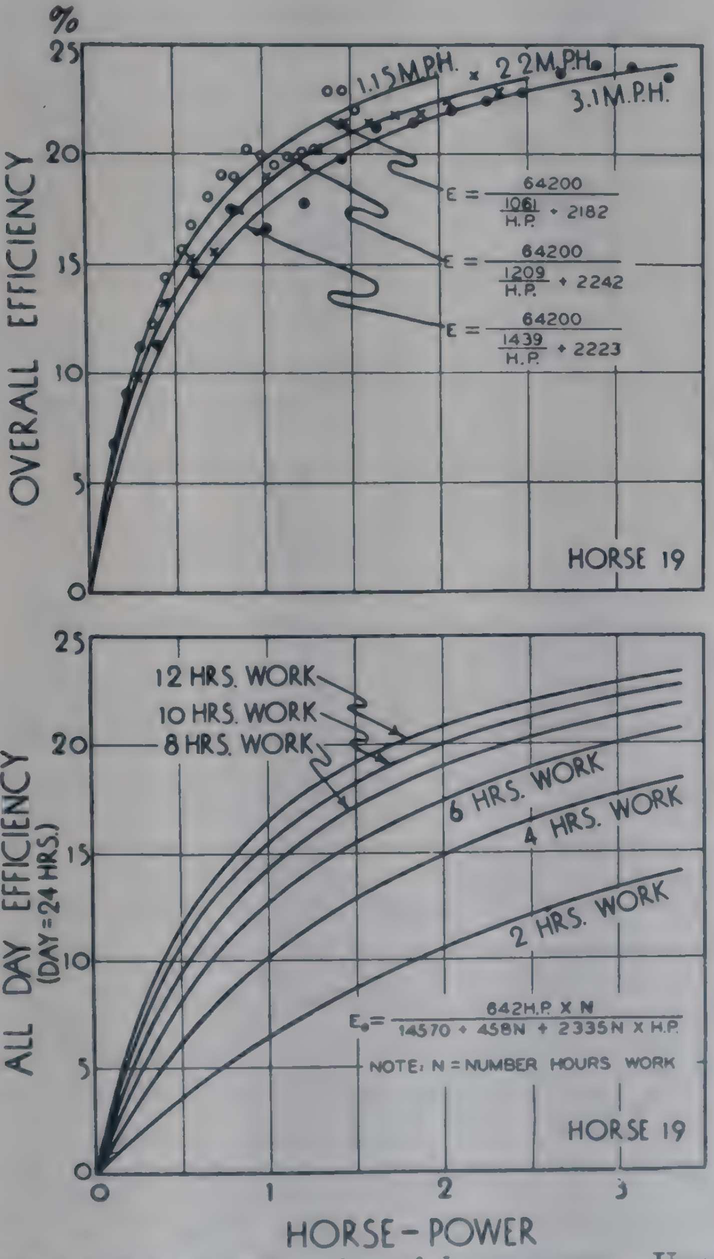

Fig. 24.10b. Overall efficiency as function of horse-power. Upper chart represents full-time work for the 3 speeds; lower chart represents part-time work, i.e., 2, 4, 6, 8, 10, and 12 hours work out of 24, all speeds combined.

Summarizing this section, 1) the rate of oxygen consumption during average walking is, approximately, double that of standing; 2) the oxygen consumption of sustained heavy work (6–10 hours/day) is 3- to 8-fold rest; 3) the *maximal oxygen consumption* is, approximately, 20-fold resting; 4) the maximal *energy* *expenditure* during maximal exertion for a few seconds is about 100-fold rest These ratios are the same for 1500-lb and 750-lb horses as for 150-lb man they are independent of body weight and perhaps of species *as such.* There are, however, considerable individual variations in this respect, and training greatly influences these ratios.

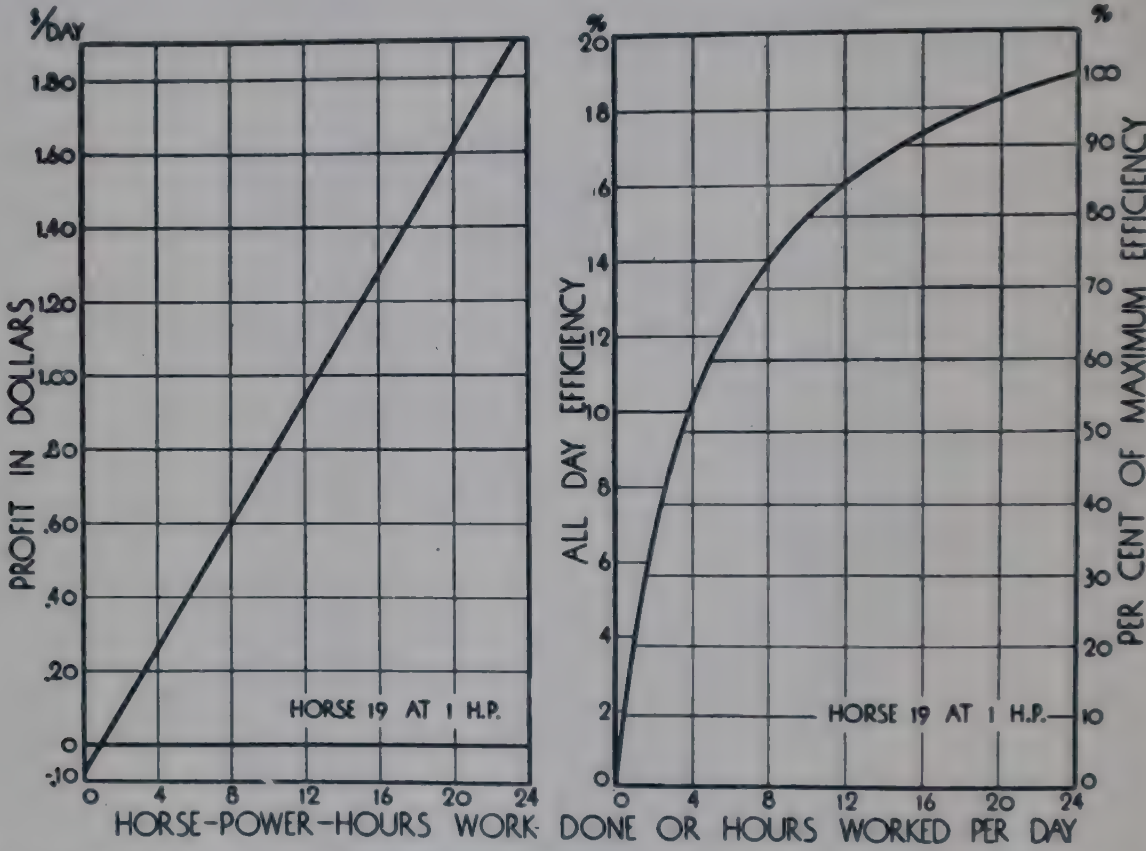

Fig. 24.10c. All-day efficiency and profit plotted against hours worked at 1 H.P. per day.

24.4: Mechanisms limiting work capacity. Muscular-work capacity is dependent on many factors such as on soundness of limbs and muscles, on body build and strength, on skill and intelligence, on temperament and ambition, and so on. These factors are more or less judgeable externally, by inspection. There are, however, also factors and aptitudes which are not externally evident, measurable only functionally. These are concerned mostly with the oxygen supply to the tissues by the cardio-respiratory system.

A distinguishing feature of animals is the onset of fatigue with increasing work, and the greater the speed of work, the more rapid the onset of fatigue. Progressive fatigue absent in "running" engines is the most conspicuous feature in running animals. A good racing horse can run a quarter mile (in 23 seconds) at the *rate* of 39 miles an hour but can never run all of the 39 miles in an hour because of encroaching fatigue after the first 30 second's run.

The speed of onset of fatigue[39] is, perhaps, the best measure of lack of work capacity and of disease. Disease has indeed been defined by impairment of work capacity.[40] Muscular work involves so many structures and functions that impairment of one of these or disturbance of the integration between them increases the speed of onset of fatigue and decreases work capacity. On the other hand, a limiting organ or function may be seriously diseased, yet the individual and observer may be unaware of it because of the masking effect of a compensatory mechanism that takes over for the duration. One organ or function may be maintained at the cost of impairment of another. Compensation may thus be associated with decompensation. Athletes sometime die when apparently in their prime because of the presence of such unsuspected, masked, serious disease.

Assuming, for the present, that muscular-work capacity is ultimately limited by the rate and efficiency of oxygen supply, one may estimate work capacity by functional tests of the several systems involved in supplying oxygen to the tissues as discussed below.

24.4.1: Pulmonary ventilation. The exhaled air per breath, "tidal air,"[41] is the capacity factor. The respiration rate is the intensity factor. If the resting tidal air is 1 liter and the resting respiration rate is 10/min, the resting pulmonary ventilation is 10 lit/min, or the minute volume of pulmonary ventilation is 10 liters. On collapsing one of the lungs the tidal air may be halved and the respiration rate doubled, thus maintaining the previous ventilation rate of 10 lit/min.

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[39] In a $1\frac{1}{4}$-mile race, one horse ran the first and second quarter miles at 24.25 sec each; the third quarter mile at 24.86 sec; the fourth at 25.62 sec; the fifth at 26.05. Blake, L. L., and Brownlee, R. B., "Race horse and race track speed, an analysis of racing records." Preliminary edition, 1936, by L. L. Blake, Standard Statistics Co., 345 Hudson St., New York, N. Y. The mile record (1942) for a horse is $1{:}34\frac{4}{5}$ made by two-year-old Count Fleet. Maximal speeds are said to be run at the rate of 22 miles/hr for man (Jesse Owen ran 100 meters, that is 328 feet, at the rate 21.7 mile/hr); horse, ass, dog, 37 mile/hr (race horses have been known to run $\frac{1}{4}$ mile at the rate of 44 mile/hr). Flying is, of course, more rapid: ranging from the golden eagle 120 mile/hr, duck hawk 180 mi/hr, deer bat fly 450 mile/hr, comparable to that of an airplane. For data and literature on "Flight speed of birds," see M. T. Cooke, U. S. Dept. Agr. Cir., 428, 1937.

[40] Simonson, E., and Enzer, N., *Medicine*, **21**, 345 (1942).

[41] The *vital capacity* is the largest volume of air exhaled following the deepest inhalation. *Vital capacity* = tidal air + supplemental air. The *alveolar air*, in contact with the respiratory epithelium, is the sum of the *supplemental* and the *residual* (non-exhalable) air. The alveolar air is richer in CO_2 and poorer in O_2 than tidal air. Alveolar air in man contains 4.5–6.5% CO_2, 13–15% O_2, 80% N_2, and is completely saturated with H_2O. Pulmonary capacities cited from Dill, *et al. Science*, **85**, 409 (1937): vital capacity, 5.4 liters in athletes and 4.7 liters in non-athletic young men. Tidal air, 2.4 liters in athletes and 2.3 liters in non-athletes. Tidal air is thus 46% of the vital capacity. For a given oxygen consumption, the athletes' ventilation rate was 12% less than of the other subjects. Pulmonary ventilation at maximal work was 113 liters per minute in the athletes and 98 liters per minute in non-athletes. The respiration rate at this maximal work was 48 in the athletes and 44 in the non-athletes. The ratio of residual air to total lung volume was 0.288 in the athletes and 0.285 in the non-athletes. Most published observations on non-athletic college students at rest cite tidal air $\frac{1}{2}$ liter, vital capacity 4 liters, respiration rate 16/min. pulmonary ventilation 8-10 lit/min. Training athletic men reduces the resting respiration rate to 10/min. The values vary with size. Women, therefore, usually have lower tidal air and pulmonary ventilation.

This compensation of the halving of the capacity factor by doubling the intensity factor occurs at an extra energy cost involved in doubling the rate of chest movement for a given ventilation rate. The chest moves twice as rapidly and fatigues more rapidly.

Moreover, the compensated pulmonary system lost half of its *reserve* capacity, its safety margin, so that the compensation has been achieved only for rest or for lower work levels. The reserve is lost for higher work levels or for disease, such as for pneumonia, emphysema (in which the diffusion of oxygen through the lungs is reduced) and with the loss of the margin of safety, life becomes correspondingly more circumscribed.

This discussion shows that *the lung capacity* (*tidal air*) *at a given metabolic rate and a given temperature is inversely proportional to the respiration rate.* It is important to specify temperature because the pulmonary ventilation also has a temperature-regulating function in slightly-sweating animals above 30°C (85°F). The respiration rate increases rapidly with increasing environmental temperature in most farm animals (but not in man). The more rapid hot-weather breathing (panting) is, however, shallowed so as to maintain the ventilation rate constant (Sect. 11.5).

24.4.2: Blood circulation. In blood circulation the pulse rate is the intensity factor and the systolic output (stroke volume) is the capacity factor, corresponding, respectively, to respiration rate and tidal air in pulmonary ventilation; and the *heart capacity* (systolic output = volume of blood ejected by a contraction or systole of the left heart or ventricle) *at a given metabolic rate* (also at a given temperature and a given emotional status) *is inversely proportional to the pulse rate.*

The average resting pulse rate in adult man is approximately 70; the lowest, usually found in great athletes, is approximately 40, although one athlete, Les MacMitchell, said that his resting pulse has been at one time 31 per minute.[42] Low pulse rate is, then, in general, an index of an efficiently-functioning, powerfully-contracting heart and, therefore, probably of great work capacity. Conversely, the smaller the systolic output, that is the less blood ejected per contraction, the more rapid must be the pulse or the heart contractions to maintain the normal circulation rate, the less efficient it is, the more easily fatigued, the less reserve it has, and consequently the smaller the work capacity.

The mechanical work of and the energy expended by the heart: The average man's heart weighs about $1\frac{3}{4}$ lb and delivers blood at the rate of about 4 lit/min at rest and, perhaps, 40 lit/min during maximal exertion. The work rate of the heart is, of course the product of the blood quantity ejected and the systolic pressure.[43] Thus (Hill, Long and Lupton) if the cardiac output is 40 liters/min and the systolic pressure is 100 mm Hg, the work by the ventricle (left side of the heart) is $40 \times 100/760 = 5.3$ liters-atmospheres per minute = 128 Cal/min. Assuming an efficiency of 20 per cent, the energy expenditure by the left side of the heart is 640 Cal/min. Adding 25 per cent for energy expended by the right side, the total expended by the heart is 890 Cal/min, equivalent to 160 cc O_2/min. Assuming a 60 per cent O_2 utilization coefficient and a blood oxygen capacity of 18.5, the coronary vessels would have to supply to the heart tissues 1.5 liters blood per minute. Hill cites an example of the consumption of 5.9 liters of *oxygen* per minute involving a total heart output of 75 liters—17 gallons—of *blood* per minute, a work rate of 631 foot-pounds per minute or 0.02 H.P.

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[42] White, P. D., *J. A. M. A.*, **120**, 642 (1942): the basal pulse rates of five men were: 38, 38, 37, 37, 35, belonging, respectively, to a marathon runner, an aviator, a champion miler, a non-athletic middle-aged man with slight hypertension, with a cardiac enlargement, a champion miler. Cunningham's pulse was reported to be between 40 and 45, Les MacMitchell's 37, and Nurmi's 40

As noted above, the average man's systolic output at rest is 60 cc and the pulse rate is 67, so that in one minute the ventricle ejects 60 cc × 67 = 4000 cc, or 4 liters blood.

During maximal exertion, the cardiac output[44] is increased tenfold, to an approximate maximum of about 40 liters. The pulse, too, increases with increasing work rate; it may increase to 180 at maximal exertion in which the maximal systolic output may reach 40000 cc/180 = 222 cc, which is near the theoretical maximum since the anatomic volume of the pericardium is, in man, not over 700 cc and the volume of the left heart cannot be over $\frac{1}{3}$ of the pericardial volume, about 230 cc. It is said that the systolic output is increased as result of training, so that more blood is pumped per minute with fewer beats for a given oxygen consumption. Training affects the entire cardio-respiratory system.[45] In one case (Knehr, et al[45]) training 6 months reduced the pulse rate from 67 to 62, respiration rate from 15.1 to 14.3, pulmonary ventilation from 6.2 to 5.7 lit/min; oxygen capacity was increased from 19.8 to 20.2 and plasma chlorides from 103.6 to 105.8.

Needless to say that in addition to the left side of the heart, the ventricle, the blood also has to pass through the right side of the heart; so that the heart as a whole ejects what virtually amounts to not 4.0 but 8.0 (over 2 gallons) liters per minute at rest and not 40 but 80 liters (over 20 gallons) per minute at maximal exertion. This surprising maximal value is, of course, achievable only by rare athletes.

24.4.3: The blood.[46] With the aid of its hemoglobin, blood carries oxygen to and carbon dioxide from the tissues to the lungs where the carbon dioxide is released and the oxygen taken on. The blood makes the circuit in about a minute, the exact speed depends on body size and metabolic rate.

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[43] *Definitions*: *Systole*, period of contraction and discharge of the blood; *diastole*, period of relaxation and refilling with blood; *systolic pressure*, maximum blood pressure during the systole; *diastolic pressure*, about $\frac{3}{4}$ of the systolic pressure, minimum pressure between the heart beats at the end of the diastole. *Pulse pressure*, difference between the systolic and diastolic pressure. The *systolic output* is a function of the product of the pulse pressure and pulse rate. The systolic pressure in adult man is 100 to 150 mm; diastolic, 65–90; pulse pressure 35–55; capillary pressure 15–40.

[44] Grollman, A., "The cardiac output of man in health and disease." Thomas, 1932.

[45] Steinhaus, A. H., *Physiol. Rev.*, **13,** 103 (1933). Dill, D. B., and Brouha, L., *Le ravail humain*, **5** (1937). Christensen, E. H., *Ergeb. d. Physiol.*, **39,** 348 (1937). Taylor, C., *Am. J. Physiol*, **135,** 27 (1941). Robinson, S., and Norman, P. M., *Am. J. Physiol.*, **133,** 168 (1941). Knehr, A., Dill, D. B., and Neufeld, W., *Id.*, **136,** 148 (1942).

[46] The published blood volume is highly variable, perhaps 6% to 7% of the body weight, perhaps 5 liters in the average man's body. The fatter the individual the smaller the relative blood volume; the more muscular and the thinner, the greater the relative blood volume. Blood contains about 5 million red cells and about 8000 white cells per cubic mm, more in athletes, less in sedentary. Arterial blood contains about 19% O_2, 50% CO_2; venous blood, about 14% O_2 and 55% CO_2. The alkaline reserve the bicarbonate CO_2 obtained from blood previously saturated with CO_2 at a partial pressure of 40 mm Hg—is 50 to 80 volume per cent. The blood hemoglobin ranges from 10 to 12% in non-athletes to 15% in athletes or athletic animals. A gram hemoglobin combines with 1.34 cc O_2 so that on saturation blood contains about 20 cc O_2 (for details, see Sect. 6.4.2).

When the blood becomes oxygenated in the lungs, it is 90 to 95 per cent saturated with oxygen, containing 17 to 20 cc oxygen per 100 cc of blood, more or less depending on the hemoglobin concentration.[46] After the blood has unloaded the oxygen to the tissues, its oxygen saturation is about 30 percent; so that the blood gives off about 60 per cent of its oxygen; 60 per cent of 20 = 12 cc oxygen per 100 cc blood. At rest, 100 cc blood may unload only 30 per cent or 5 to 6 cc oxygen; during maximal exercise in well-trained athletes, it may unload 70 per cent or 15 cc oxygen.

The intensity factor of the blood is, then, the arterio-venous oxygen difference; the capacity factor, the amount of hemoglobin.[46] The coefficient of oxygen utilization (Krogh) is the ratio of the arterio-venous difference (or oxygen transport) to volume percent of oxygen in the blood (oxygen capacity).

A high blood capacity like a large pulmonary or cardiac capacity indicates a large oxygen-reserve power. Diving animals,[47] some of which (whales) can remain submerged 2 hours, or even those (beavers, seals) that can remain submerged for one-half hour have unusually large blood volumes and hemoglobin concentrations, including muscle hemoglobin, perhaps double those of non-diving species. High-altitude dwellers[48] (such as the llama, vicuna, S. American ostrich, and native man, too) have larger quantities of hemoglobin than low-altitude dwellers. But, as previously noted, individuals within the species and under the same conditions also differ in their hemoglobin content and in the percentage of oxygen they can unload on their circuit (for fuller discussion see Sect. 6.4.2).

24.4.4: Oxygen debt. As previously explained (Ch. 6), biologic oxidation is a stepwise process, the initial stages of which do not involve the participation of oxygen, illustrated by the (anaerobic) conversion of glucose to lactic acid. When, therefore, in maximal exertion for several seconds (as in the 60-yard dash in man, $\frac{1}{4}$ miles dash in the horse, or in the 10-second horse-pulling contest) the energy expenditure is perhaps five-fold the maximal capacity of oxygen supply, the energy is obtained from anaerobic oxidation. Intermediate products are formed (lactic, phosphoric, and pyruvic acids) which are oxidized during the recovery phase. Phosphocreatine and adenosine pyrophosphate are also decreased during the exercise and reformed during the recovery. The oxygen debt is, then, measured by the oxygen increment above normal rest oxygen consumption during the recovery or resting phase. The oxygen debt is known (Ch. 6) to have risen in a 70-kg athlete to 19 liters and the lactic acid to 114 gm ($\frac{1}{4}$ lb) or to 0.32 per cent. (The lactic acid content in resting human blood is 0.01–0.02 per cent.) One liter of the oxygen increment consumed during recovery is often assumed to be equivalent to the removal of 7 to 8 gm lactic acid or to its re-conversion to glycogen, although the oxygen debt may be alactic.[49]

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[47] Irwing, L., *Physiol. Rev.*, **19**, 112 (1939).

[48] Dill, D. B., "Life, heat and altitude," Harvard Press, 1928. Hall, F. G., Dill, D. B., and Barron, E. S. G., *J. Cell. and Comp. Physiol.*, **8**, 301 (1936).

Athletes (also diving animals and mountain dwellers) are thus distinguished not only for their ability to perform much work without going into oxygen debt but also to go into great oxygen debt when the necessity arises. They are thus provided with two supplementary reserves or mechanisms for survival in oxygen-lack emergencies.

24.4.5: Coronary circulation. The astonishingly high rate of work the heart is capable of performing, pumping 40 liters of blood a minute against a very considerable pressure, is, of course, conditioned on a heart muscle well supplied with oxygen as well as with fuel. As indicated by Hill's data cited above, the heart must have for its own use alone, at maximal work, not less than 1.5 liters of blood a minute (assuming a 60 per cent oxygen utilization). This special blood supply for nourishing the heart muscle itself is furnished by the coronary arteries. If the coronary arteries develop a defect, the work capacity of the heart muscle is correspondingly reduced—the heart cannot work without a plentiful oxygen (blood) supply. Attempt to work with an inadequate coronary blood supply results in inadequate oxygenation, in ischemia of parts of the heart muscle which gives—to persons whose nerves are sensitive to such sensations—the "heart" pain, angina pectoris. As this pain is frequently localized in the pit of the stomach, it is sometimes mistaken for "acute indigestion" in man or "colic" in horses. Some sufferers from inadequate coronary circulation are apparently insensitive to ischemic pain signals and die suddenly, without warning, on some sudden exertion, or excitement, or over-eating (especially on fermentable forage or food).

It is obvious that athletes and others, such as race horses and dogs, indulging in maximal effort must be endowed with phenomenal coronary-artery systems although sudden death in athletes and race horses may occur due either to accidental coronary obstruction (coronary thrombosis) or to insensitiveness to anginal pains which keeps them ignorant of their coronary inadequacy, leading to exertion beyond their cardiac capacity.

The coronary arteries tend to deteriorate with increasing age[50] although very aged individuals often have youthfully-appearing and functioning coronaries. Indeed, the youthful coronaries may be the reason for their survival to an advanced age. The early deterioration of the coronaries may depend not only on their hereditary quality but also on the neuroendocrine system which controls the caliber of these arteries. This is inferred from the large incidence of early coronary damage in highly-strung individuals. Overproduction of adrenalin is said to be an influencing factor (Raab). Excessive dietary fat,

[49] Lundsgaard, E., *Bioc. Z.*, **117**, 51 and 162 (1930). Margaria, R., Edwards, H. T. and Dill, D. B., *Am. J. Physiol.*, **106**, 689 (1933), and **107**, 681 (1934).

[50] Robinson, S., *Arbeitsphysiol.*, **10**, 251 (1938).

especially rich in cholesterol, is said to produce atherosclerosis[51] (rather than arteriosclerosis).

24.4.6: Body-temperature regulation.[52] Hard muscular work is, of course, associated with correspondingly rapid heat production, thus placing the temperature-regulating mechanisms under stress. The extra heat dissipation is associated with the shunting of blood to the surface, leaving less blood in the interior, with consequent increase in pulse rate which may lead to heart failure (heat exhaustion, heat stroke, sun stroke). "Heat cramps," muscular pains, are associated with loss of salt in the sweat.

The cooler the environmental temperature, within limits, the lower the strain of heat dissipation and, therefore, the higher the attainable work rate. Conversely, the higher environmental temperatures, especially above 30°C (85°F), are less favorable for hard work and indeed dangerous at the later ages (Chs. 11 and 18).

24.4.7: Nutrition. It is believed that carbohydrate is the best fuel for muscular work. The superiority of carbohydrate to fat as fuel is due to several factors, including, 1) greater readiness of mobilization of carbohydrate for muscular work; 2) about 7 per cent less oxygen is required to obtain unit energy from carbohydrate than fat (the thermal equivalent per liter oxygen is 5.05 for carbohydrate and 4.69 for fat); 3) it is believed[53] that before oxidation for muscular work, fat is converted to carbohydrate, involving a 10 per cent energy loss in the conversion. (Hill[54] believes that for peak effort carbohydrate is the only fuel.) Whatever the theory, Christensen[55] observed that men engaged in "steady-state" maximal work succeeded in continuing the work for 4 hours on a high carbohydrate diet, but only 1½ hours on a high fat diet. Moreover, an hour of such work on the high fat diet was followed by accumulation of acetone bodies in the blood.[56] Dill[57] observed that a dog could run on a treadmill 17 hours when supplied with glucose, but only 4 hours when not so supplied, and compelled to live on body fat. The blood sugar of the dog not receiving glucose reached the low level of 50–60 mg per cent at the time of exhaustion, about half the normal blood-sugar level.

There is no general agreement on the question as to whether fat can be used as muscle fuel[58] nor on the optimal carbohydrate-to-fat proportions in the body-fuel mix. Henderson and Haggard[59] reported that fat furnished about $\frac{2}{3}$ of the energy expended by their Yale oarsmen; that is, sugar is not the sole fuel of muscular energy. However, they believe that sugar is the fuel most immediately available for muscular work and that it would be helpful to the "wind" and for avoiding overtraining if athletes were furnished enough carbohydrates to maintain an R.Q. of 0.85 to 0.9 (when carbohydrates would contribute 50 per cent to 65 per cent of the total energy).

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[51] Cowdry, E. V., "Arteriosclerosis," Macmillan, 1933, and "Problems of ageing," William and Wilkins, 1939. Brody, S., *Ann. Rev. Bioc.*, **4**, 383 (1935).

[52] Ch. 11, and Dill, *Physiol. Rev.*, **16**, 262 (1936). Dill, *et al.*, *Arbeitsphysiol.*, **4**, 508 (1931). Christensen, E. H., *Id.*, p. 154. Lefévre, J., et Auguet, A., *Annal. physiol. et physicochim. Biol.*, **9**, 1103 (1933).

[53] Krogh, A. and Lindhard, J., *Bioc. J.*, **14**, 290 (1920).

[54] Hill.[16]

[55] Christensen, E. H., *Arbeitsphysiol.*, **4**, 128, 145, 170, and 175 (1931); **5**, 463 and 479 (1931); **7**, 108 and 121 (1933–4).

[56] Christensen.[55] Himwich, *et al.*, *Am. J. Physiol.*, **83**, 92 (1927); **88**, 663 (1929); *J. Biol. Chem.*, 57, 353 (1923).

[57] Dill, D. B., Edwards, H. T., and Talbot, J. H., *J. Physiol.*, **77**, 49 (1932).

[58] Rapport, D., "Interconversion of foodstuffs," *Physiol. Rev.*, **10**, 349 (1930). Carpenter, T. M., "Fuel of muscular activity," *J. Nut.*, **4**, 281 (1931); Gemmill, C. L., "Fuel for muscular exercise," *Physiol. Rev.*, **22**, 32 (1942).

These authors quote approvingly the well-known dictum[60] that "in the living body, fat burns only in the flame of sugar," meaning that with deficiency of sugar, oxidation of fat is incomplete. They suggest that it would be advantageous to raise the R.Q. by "eating a quarter of a pound of some simple candy, such as peppermint creams, a half to three-quarters of an hour before any prolonged contest" (Sect. 7.6).

Dill[61] does not think that there is carbohydrate deficiency in blood under ordinary conditions of hard sustained work.[62] This he infers from the fact that steel workers show no symptoms of ketosis, the usual test for fat preponderance (i.e., carbohydrate deficiency) in the oxidation mix; he attributes the favorable effect of refreshments in mid-morning and mid-afternoon[63] to psychological rather than nutritional factors. However, heavy work, especially under conditions of emergency, makes heavy inroads on the carbohydrate level, and glucose intake should be very helpful. The collapse of marathon runners has often been attributed to carbohydrate depletion.[64]

Recently publicity was given by gelatin manufacturers to a report that gelatin (washed down with orange juice) increased the work capacity of bicycle riders.[65] This research was motivated by that fact that $\frac{1}{4}$ of gelatin is glycine and that glycine enters into phosphocreatine which is supposed to furnish energy for muscular contraction (Ch. 6). However, all proteins are rich in glycine (Sect. 20.7), vigorous muscular exercise can take place when the phosphocreatine concentration is very low, and recent data do not indicate that gelatine is helpful in muscular contraction.[66]

Vitamin C may become a limiting factor in muscular work because, like salt,[67] it is lost in sweat and deficiency may cause muscle pains during strenuous work.[68] The pains were relieved by feeding 300 mg ascorbic acid a day (contrasted to the "standard" 75 mg). Horses synthesize ascorbic acid but perhaps not sufficient for their needs under conditions of prolonged hard work in a hot climate. A common salt solution of 0.9 per cent is the usual prophylactic against excessive salt loss in the sweat of hard working man in hot environments, which causes muscular pain (heat cramp).

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[59] Henderson, Y., and Haggard, H. W., *Am. J. Physiol.*, **72,** 264 (1925).

[60] Shaffer, P. A., *et al.*, *J. Biol. Chem.*, **47,** 433 and 449 (1921); **49,** 143 (1921); **54,** 399 1922); **61,** 585 (1924); **66,** 63 (1925); at least $\frac{1}{2}$ molecule of glucose must be oxidized for each molecule of fatty acid or acetoacetic acid; if less glucose is available, the fat oxidation stops at the acetoacetic acid stage. Glucose-forming amino acids and glycerol are, like glucose, antiketogenic, but to a smaller extent. Certain amino acids (such as tyrosine, phenylalanine, leucine) are, like fats, ketogenic.

[61] Dill, D. B., "Industrial fatigue." *Industrial Medicine*, July, 1939.

[62] Haldi, J., *et al.*, *Am. J. Physiol.*, **121,** 123 (1938). Cited by Dill.

[63] Haggard, H. W., and Greenberg, L. A., "Diet and physical efficiency." Yale Press, 1935.

[64] Best, C. H., and Partridge, R. C., *Proc. Roy. Soc.*, **105B,** 323 (1929). For reviews, see Schneider, E. C., "Physiology of muscular activity," 1933. Boje, O., *Skand. Arch. Physiol.*, **71,** 61 (1935).

[65] Gay, G. B., *et al.*, *Proc. Soc. Exp. Biol. and Med.*, **40,** 157 (1939).

[66] King, E. Q., McCaleb, L. B., Kennedy, H. F., and Klump, T. G., *J.A.M.A.*, **118,** 594 (1942).

The need for oxidation-reduction vitamins (Ch. 6) in general tends to be directly proportional to the rate of work, that is to the rate of oxygen consumption. Thiamine is a conspicuous member in this category. Other methods of improving performance are widely but fruitlessly discussed.[69]

In this connection a word may be said concerning hormone administration. Thyroid administration to a hypothyroid animal will, of course, increase its work capacity; but its administration to normal animals is likely to decrease work capacity. It is known that the energy cost of work is much higher and efficiency lower in hyperthyroid than in normal individuals,[70] perhaps because of the high circulation rate in the hyperthyroid.

Likewise, as regards adrenal hormones. The administration of adrenalin to adrenal demedullated rats or to adrenalectomized rats treated with either adrenal steroid or glucose increased the rate of work of rats;[71] but it is not certain that adrenal-cortex administration to normal animals modifies work ability, willingness, or efficiency.[72] Nor is benzedrine or amphetamine, a drug related to adrenalin and widely publicized for its effect on "intelligence," helpful.[73] Adrenalin may, however, facilitate carbohydrate utilization. Its administration to a *fasting* man working at a moderate rate increased carbohydrate utilization "more than one-half over the corresponding period in the control experiment."[74]

24.5: Measuring work capacity. The preceding section discussed the factors which, singly or in combination, limit work capacity: pulmonary ventilation, blood circulation, oxygen capacity of blood, oxygen debt, coronary circulation, body-temperature regulation, nutrition. Some of these factors were resolved into capacity and intensity components. Stamina, reserve power, endurance appear to be directly proportional to the capacity components of these factors, such as to systolic blood output, tidal air exhalation, quantity of hemoglobin (blood), caliber of the coronary vessels. Some of these components, such as tidal air, respiration rate, and pulse rate are easily measured. Perhaps the most important of these, namely systolic output, is not easily measured in horses, and not even in man.[75] As a result, attempts were made to estimate indirectly the systolic output and circulatory conditions based on some reasonable assumption, such as that the systolic blood output is directly proportional to the pulse pressure (difference between systolic and diastolic pressures), and that the circulation trend is proportional to the product of pulse pressure and pulse rate, as indicated by the equation[76]

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[67] Dill, D. B., *Physiol. Rev.*, **16**, 262 (1936), and Harvard Alumni Bull., Oct. 20, 1939.

[68] Brunner, H., *Schweiz. med. Wochenschr.*, **71**, 701 (1941).

[69] Boje, O., Doping; *League of Nations*, **8**, 439 (1939), and *J. A. M. A.*, **115**, 1281 (1940). The uses of phosphates, ammonium chloride, oxygen, lecithin, liver preparations, sodium bicarbonate, cocaine, caffeine, amphotamine sulfate, valerian, bromides, barbituric acid, digitalis, glyceryl trinitrates, metrazol, etc. are discussed. However, any substance capable of stimulating the body to exertion beyond the normal limits of fatigue set by the body is most likely to be injurious in the end, and, therefore, none of these is recommended.

[70] Plummer, H. S., and Boothby, W. M., *Am. J. Physiol.*, **63**, 406 (1923). Boothby and Sandiford, *J. A. M. A.*, **81**, 795 (1923).

[71] Ingle, D. J., and Lukens, F. D. W., *Endocrinology*, **29**, 443 (1941).

[72] Hall, V. E., *Am. J. Physiol.*, **121**, 537 (1938). Hitchcock, F. A., Grubbs, R. C., and Hartman, F. A., *Id.*, p. 542. Dill, D. B., *et al.*, *Id.*, p. 549.

[73] Dill, D. B., *et al.*, *Aviation Medicine*, **11**, pp. 1–16 (1940).

[74] Dill, D. B., *et al.*, *Am. J. Physiol.*, **111**, 9 (1935), and **130**, 600 (1940).

$$\text{Circulation-rate index} = \text{pulse pressure} \times \text{pulse rate}$$

or by a modification of the above as:[77]

$$\text{Circulation-rate index} = \frac{\text{pulse pressure} \times \text{pulse rate}}{\text{arterial pressure}}$$

The above index is in fair agreement with experimentally determined values in normal (but not in cardiac-defective) individuals.[78]

Another such indirect method, widely used, was suggested by Fick (1870) which assumes that the blood output by the heart *per minute* (minute heart volume) is the O_2 consumption per minute divided by the arterio-venous O_2 difference (or the CO_2 production divided by the arterio-venous CO_2 difference); and the systolic output is, then, heart output per minute divided by the pulse rate.

It is clear that we are not yet in a position to estimate the stamina of an animal from each of the component factors. How, then, shall we go about formulating a test of physical capacity?

The most obvious approach is by way of measuring the performance of the body as a whole, integrated performance.

Performance of a given *exercise* is not a good test of stamina because performance also depends on skill (training), intelligence, temperament ("will" to succeed), and so on.

Maximal performance tests for a few seconds, exemplified by the 60-yard sprint by man, $\frac{1}{4}$-mile sprint by horses, or by horse pulling contests previously described, are tests for neuro-muscular skill and muscular strength but not necessarily stamina or endurance because the energy for maximal exertion for 5 to 30 seconds is derived from anaerobic oxidation, that is, not directly dependent on the cardio-respiratory system and yet it may overtax this system and lead to a break-down. The usual dynamometer measures of strength test specialized groups of muscles while stamina and endurance are usually proportional to the cardio-respiratory capacity and to the stability of the nervous system[79] which controls the pulse rate, blood pressure, distribution of blood and related integrative phenomena. Athletes, improving with training in all the usual strength and skill tests, often suffer nervous break-downs on approach to their apparent prime condition, due to some integrative fault. The body has many compensating or homeostatic mechanisms (Ch. 10); a weak organ or function is often maintained or compensated perhaps at the cost of impairment or decompensation of another organ. This may explain, for example, the occasional rejection of athletes for the military service.

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[75] For exhaustive descriptions of methods and history of measuring systolic output, see Grollman.[44]

[76] Erlanger, J., and Hooker, D. R., *Johns Hopkins Hosp. Repts.*, **12**, 147 (1904).

[77] Liljestrand, G., and Zander, E., *Z. Exp. Med.*, **59**, 105 (1928).

[78] Neilson, H. E., *Acta Medica Skandinavica*, **91**, 12 (1937).

The problem of devising a criterion of physical fitness is a very difficult one, especially in animals who do not cooperate with the investigator. Thus, the widely-used Schneider-fitness test,[80] based on adjustment speed to work and rest, and on standing-lying differences in blood pressure and pulse rate, is not easily applied to horses or other farm or laboratory animals. Moreover, the Schneider test makes but very slight demand on the cardiovascular reserve.[80a] There is no satisfactory relation between basal pulse rate, sitting pulse rate, and physical fitness for strenuous exertion in normal individuals, and emotional factors have a greater effect on pulse than cardiac reserve.[80b]

Let us consider possible tests which promise to be applicable to farm and laboratory animals as well as to man.

24.5.1: Maximal oxygen consumption. The maximal steady-state oxygen consumption represents the maximal rate of energy expenditure when the metabolic functions (O_2 consumption, CO_2 production, pulse and respiration rates, ventilation rates, etc.) are steady, that is, constant and, therefore, not involving the incurrence of a cumulative oxygen debt. Reference was made to Robinson, Edwards and Dill who observed a maximum steady-state oxygen consumption of 5.1 liters/minute, 21.4 times basal, in a famous athlete (Lash), as contrasted to 14.5 times basal in the best untrained subject.

In this connection one may note the interesting observation[81] that the carbon dioxide percentage in expired air rises with increasing work rate up to a certain work-rate level, then begins to decline. This may be associated with the phenomenon of the "second wind" when, perhaps, the respiratory center in the brain loses its sensitiveness to further CO_2 concentration and perhaps loses control of the CO_2 composition of expired air. Would this inflection in the CO_2 concentration curve serve as a definition of maximal work rate?

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[79] Of all the tissues and systems, the nervous is most sensitive to oxygen lack, illustrated by "blackouts," and dizziness during rapid change in altitude (in airplanes, submarines, elevators, or even on rapid change in position, especially when whirling). One reason for the success of diving animals in remaining submerged in water is that they have mechanisms for hoarding the oxygen and shunting it to the nervous system (see Irving.[47]). The muscles, but not nerves, can get along for sometime without oxygen. The loss of sensitiveness in finger tips, etc., is one of the first signs of an ischemic or anemic condition

[80] Schneider,[34] and *J. A. M. A.*, **74,** 1507 (1920).

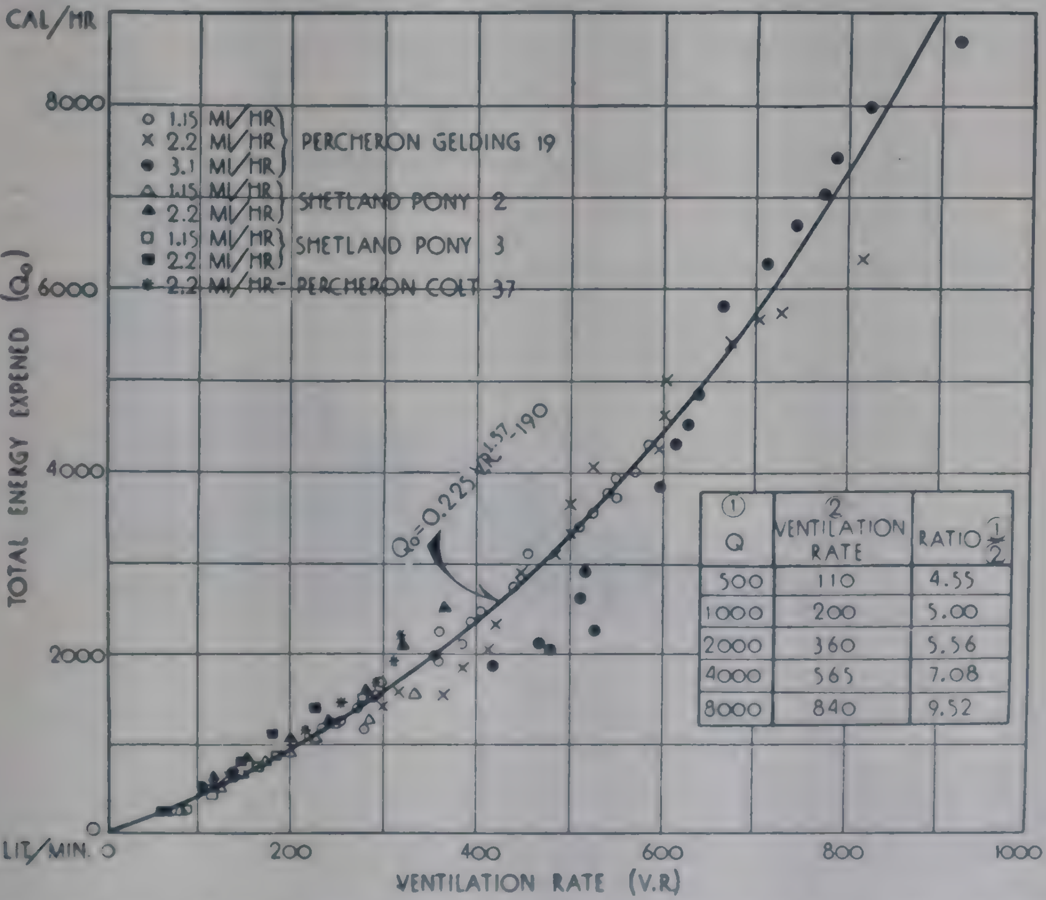
[80a] Feil, H., "The Schneider index as modified by circulatory disease," *Am. Heart J.*, **26,** 1 (1943).

[80b] Brouha, L., *et al.*, "Resting pulse and blood pressure in relation to fitness," *New Engl. J. Med.*, **228,** 437 (1943).

[81] Briggs, H., *J. Physiol.*, **54,** 292 (1920).

For practical purposes maximal steady-state effort may be defined by the maximal work without incurring an oxygen debt.

To illustrate the practical value of knowing the maximal oxygen-consumption rate, one may note that a large fraction of the American population following age 50 years has a maximal oxygen consumption rate twice resting. This means that their maximal exertion cannot exceed that of walking at a moderate rate. This may be contrasted to lumber-camp work involving a steady oxygen consumption eight-fold basal; or steady fast running involving an oxygen consumption of, perhaps, 14-fold basal.



① Q	2 VENTILATION RATE	RATIO $\frac{1}{2}$
500	110	4.55
1000	200	5.00
2000	360	5.56
4000	565	7.08
8000	840	9.52

Fig. 24.11. Interrelation between oxygen consumption and pulmonary ventilation. The ventilation rate lags behind the oxygen consumption rate.

24.5.2: Maximal pulmonary ventilation. Since the rate of pulmonary ventilation tends to be proportional (but not linearly, see Fig. 24.11) to the rate of oxygen consumption or carbon dioxide production, the pulmonary ventilation rate may be taken as index of physical fitness. When the maximal pulmonary ventilation rate is only twice that of rest, the individual is in poor condition. As previously noted,[41] Robinson, Edwards and Dill observed that three great athletes (Lash, Venzke, and San Romain) attained during maximal-effort work a ventilation rate of 113 liters/minute, 15 to 22-fold the average resting ventilation rate of 5 to 8 liters/minute.

Poor condition of the lungs with low rates of oxygen diffusion is compensated by higher pulmonary ventilation rate for a given metabolic rate. The resting ventilation rate in emphysemia, asthma, bronchitis, pneumonia may be two to three times that of normal individuals. The *ventilation reserve*[82]—the difference between the resting and maximal ventilation—is thus less in such patients than in normal individuals.

24.5.3: Rates of adjustment to work and rest and the speed of exhaustion. It, naturally, takes a little time following the go-signal for the rates of oxygen consumption, pulse, pulmonary-ventilation, blood pressure, etc., to reach the steady state. Likewise, when exercise stops, it takes a little time for the rates of oxygen consumption, pulse, blood pressure, etc. to decline to the starting level. Individuals differ in the rates with which the adjustments are made: and the fitness of the individual, of his homeostatic mechanisms (Ch. 10), may be measured by the adjustment speeds. This is one phase of the Schneider test as it relates to the adjustment of pulse rate and blood pressure (redistribution of the blood flow). The speed of incurrence of and recovery from oxygen debt, acid accumulation, and hypoglycemia, might be included in this recovery-test category.

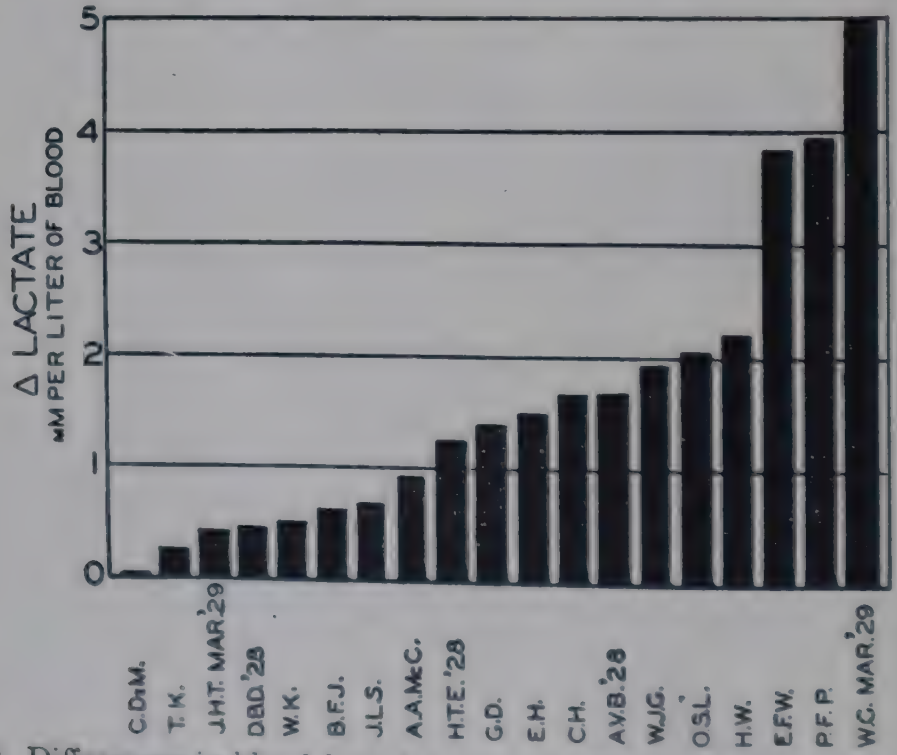


Fig. 21.12. Differences in blood lactate accumulation in 19 men of varying physical ability after 20 minutes exercise expending about ten-fold resting energy. Subjective fatigue feeling paralleled lactate concentration. From D. B. Dill, A. V. Bock, H. T. Edwards and P. H. Kennedy, *J. Indust. Hygiene and Toxicology*, *18*, 419 (1936).

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[82] Knipping, H. W., *Klin. Wochsch.*, **17**, 1097 (1938). Kaltreider, N. L., and McCann, W. S., *J. Clin. Inv.*, **14**, 81 (1935). (The pulmonary reserve in emphysema patients is about ¼ that of normal individuals.)

Another aspect of the same problem is the tiring speed, which Dill, et al. measured by the blood lactate level after 20 minutes exercise at an energy expense 10-fold that of rest. Fig. 24.12 shows that the blood lactate ranged from 0.1 mM/lit in a famous athlete to 5.0 mM/lit in an individual in poor condition. The subjective feeling of fatigue appeared to parallel the lactate accumulation. The better the condition the higher the cardio-respiratory, the oxygen-supplying, reserve. The accumulation of blood lactate is, of course, due to inadequate oxygenation. The normal resting blood lactate is 10 to 20 mg per cent (about 0.1 to 0.2 millimols per liter, since the m.w. of lactic acid is 90.08). A cardiac patient at rest has been reported[83] to contain 71 mg per cent lactic acid, and the greater the cardiac disability the greater the blood lactate concentration following a given fairly strenuous exercise. Dill[84] suggested that exhaustion during work at a high temperature comes when the accumulation of lactic acid in the heart reaches a limiting value.

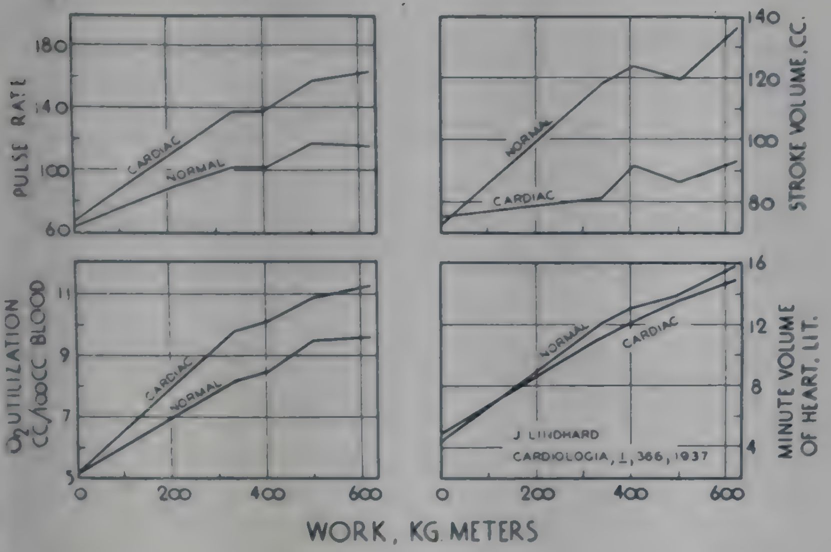

Fig. 24.13. Compensation of low systolic output or stroke volume (upper right) by high pulse rate (upper left) and high oxygen utilization (lower left) resulting in a normal minute volume of blood output (lower right).

Cardiac patients may not differ superficially from normals by the rates of oxygen consumption, pulmonary ventilation, or lactic acid accumulation at reasonably low work rates. Thus Fig. 24.13 shows wide differences in systolic output of two individuals, yet virtually the same minute volumes of blood circulation due to the compensatory effects of higher pulse rate and oxygen utilization. The resting pulse rate is, except in special cases, not an index in normal individuals, especially as emotion profoundly affects the pulse.

One of the best available measures of physical fitness is the speed of recovery of the pulse rate following a standard exercise sufficiently intense that no one in the given class can maintain a steady state for over 5 minutes. There is a large literature on this type of test,[84a] the latest being by Brouha and associates, done mostly at the Harvard Fatigue Laboratory[84b]. As used by these investigators for humans, the subject steps up and down a 20-inch platform 30 times a minute for 5 minutes, unless stopped before by exhaustion. The pulse is counted from 1 to 1½ minutes, 2 to 2½ minutes, 3 to 3½ minutes after work stops. The fitness index is given by the ratio of 100 × work in seconds to 2 × sum of heart rates taken 1–1½, 2–2½, and 3–3½ minutes after exercise. A ratio below 55 is poor and above 90 is excellent. Needless to say that allowances must be made in this test for differences in size, age, sex, environmental temperature, and so on. We are attempting to use the rate of decline in pulse rate as an index of endurance in jack stock, mules, and horses.

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[83] Harris, I., Jones, E. W., and Alfred, C. N., *Quart. J. Med.*, **4**, 407 (1935). Meakins, J., and Long, C. N. H., *J. Clin. Inv.*, **4**, 273 (1927).

[84] Dill, D. B., Edwards, H. T., Bauer, P. S., and Levenson, E. J., *Arbeitsphysiol.*, **4**, 517 (1931).

24.5.4: Oxygen pulse per unit weight. Our[85] research on work-capacity indices has been chiefly concerned with the oxygen pulse per unit body weight.

The *oxygen pulse* is the oxygen consumed per heart beat. The greater the blood volume pumped by the heart per pulse for an animal of a given weight the slower the pulse rate. The oxygen pulse per unit body weight is, then, our index or the systolic output, or heart capacity, which is the usual limiting factor in hard muscular work.

We shall use the following symbols in deriving our oxygen-pulse body-weight equation:

O_2 = rate of O_2 consumption in cc/min.
f = pulse rate or frequency per minute.
W = body weight in Kg.

The basal oxygen consumption in mature animals of different species, ranging from mice to elephants, is given by the equation (Ch. 13)

$$O_2 = 10.2W^{0.73} \tag{1}$$

Employing Clark's[86] compilation and analysis of pulse rate data, the corresponding pulse-rate-weight equation is

$$f = 217W^{-0.27} \tag{2}$$

Dividing equation (1) by (2), we obtain

$$\text{Oxygen pulse} = \frac{O_2}{f} = \frac{10.2W^{0.73}}{217W^{-0.27}} = 0.047W^{1.00} \tag{3}$$

indicating that the oxygen pulse, O_2/f, is directly proportional to body weight, to $W^{1.00}$, and not to surface area or to $W^{2/3}$ or $W^{3/4}$. Equation (3) could be derived theoretically, by dimensional analysis (Chs. 13, 17). The graphic relation between O_2, f, and W is shown in Fig. 24.14a.

[84a] Taylor, C., *Am. J. Physiol.*, **135**, 27 (1944).

[84b] Brouha, L., *et al.*, *Rev. Canadienne de Biol.*, **2**, 86 (1943); *Yale J. Biol. and Med.*, **15**, 657, 671, 679, 689, 769, and 781 (1943).

[85] Kibler, H. H., and Brody, S., Univ. Mo. Agr. Exp. Sta. Res. Bull., 367, 1943.

[86] Clark, A. J., "Comparative physiology of the heart." Macmillan, 1927.

Equation (3) may, of course, be written

$$\frac{O_2/f}{W} = 0.05 \qquad (4)$$

indicating that the ratio of oxygen pulse to body weight tends to be the same in mature animals of all the species represented by equation (1) and (2), from mice to elephants. If the oxygen-pulse to body weight index is 0.05, the animal probably has an average work capacity; if below 0.05 its work capacity is below the average; if it is above 0.05, its work capacity is above the average.

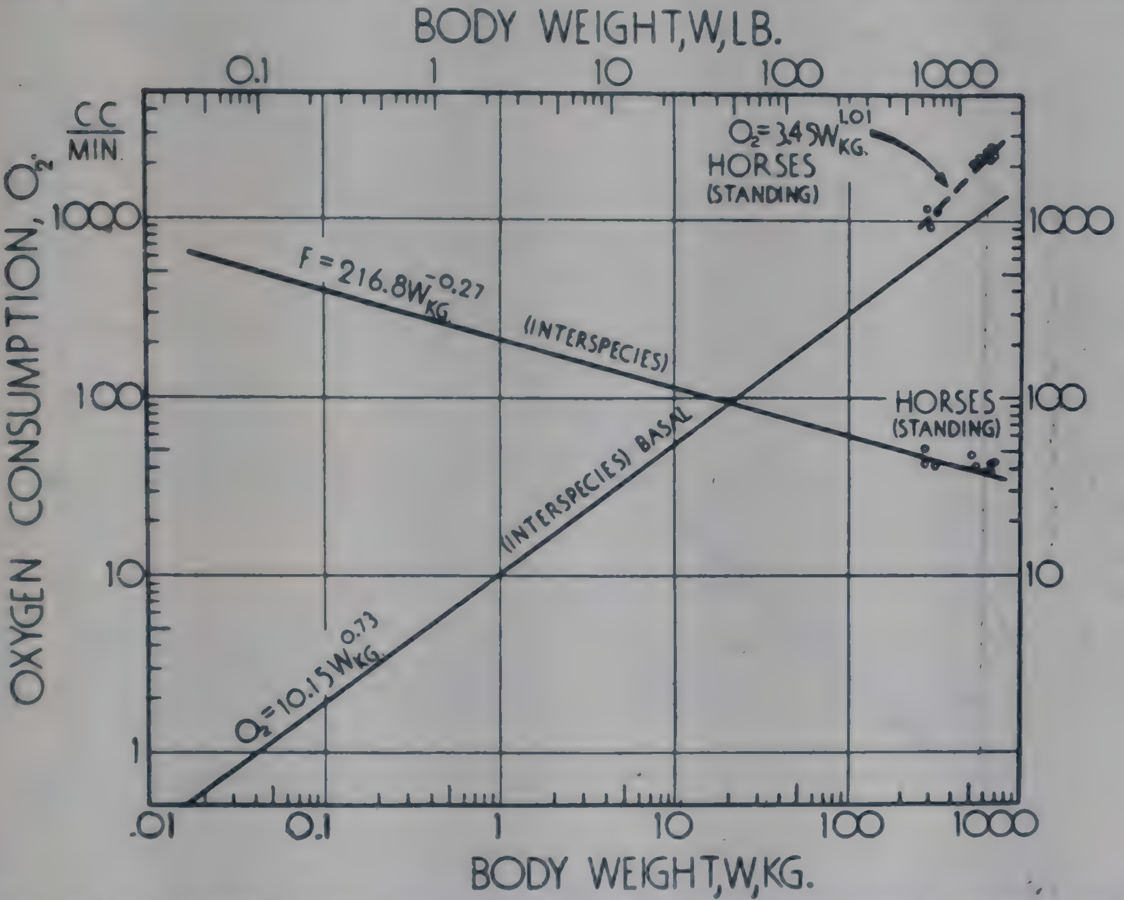

Fig. 24.14a. Oxygen consumption and pulse rates as functions of body weight.

Fig. 24.14b shows that the oxygen pulse plots practically linearly (the slope on log-log paper is 0.99, nearly 1.0) against body weight and that athletic men, horses, and dogs are above the fitted average line while non-athletic man, beef cattle, "tame" rabbits, and guinea pigs are below the line.

By this type of reasoning, the oxygen pulse, defined by Henderson and Prince[87] for man alone as the outstanding factor conditioning "total energy which a man can command for the most strenuous moments of life" was generalized by us to include all species, from mice to elephants, a promising tool for comparative bioenergetics, especially for estimating work capacity, particularly under emergency.

[87] Henderson, Y., and Prince, A. L., *Am. J. Physiol.*, **35**, 106 (1914).

A useful derivation from the oxygen-pulse equation (3) in another connection is

$$\frac{O_2}{W} = 0.05f \tag{5}$$

indicating that the basal *oxygen consumption per unit weight in mature animals of different species is directly proportional to the pulse rate;* or that the basal

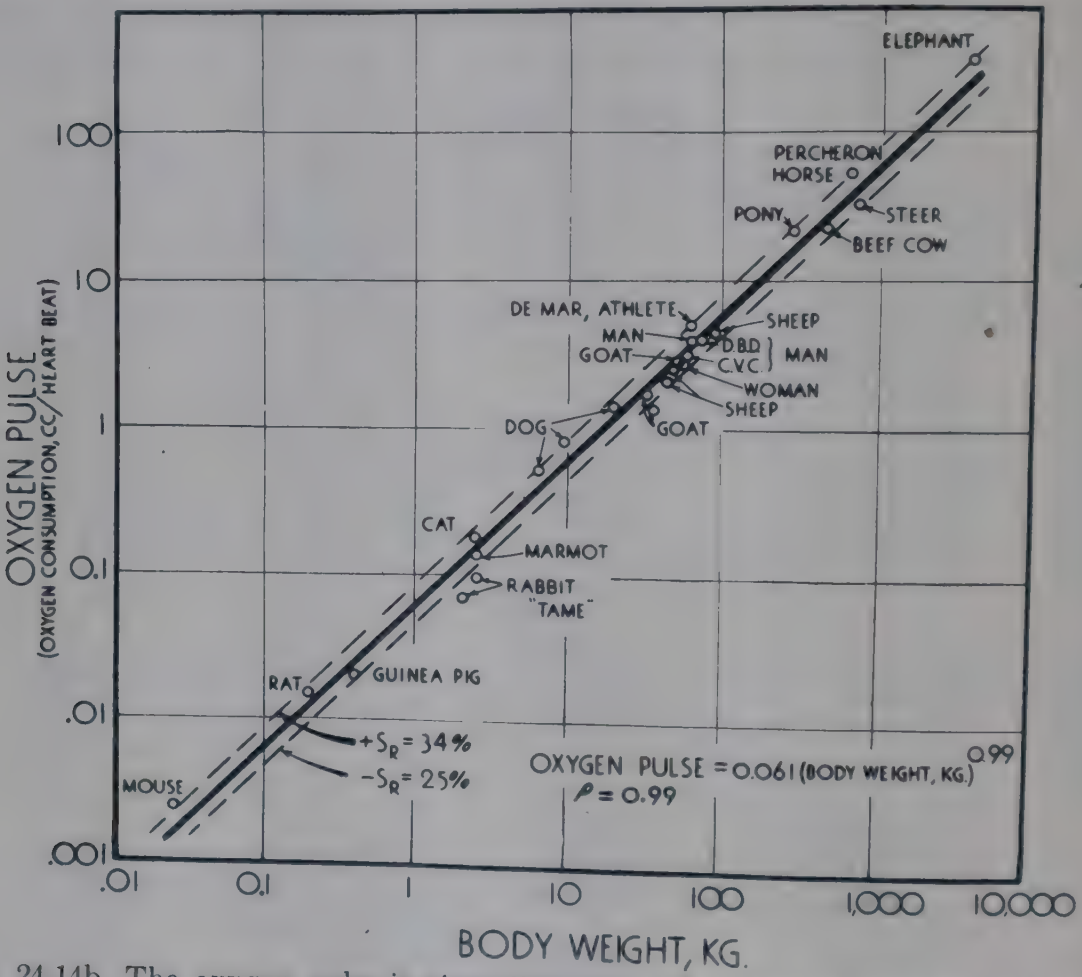

Fig. 24.14b. The oxygen pulse is virtually a linear function of body weight; it is directly proportional to weight (not to surface, etc.). See reference 85.

oxygen consumption in mature animals of different species is directly proportional to the product of weight and pulse rate:

$$O_2 = 0.05fW \tag{6}$$

Returning to the consideration of the oxygen-pulse index, the following table lists values of the resting or basal oxygen pulse per kilo of different animals from mice to elephants. The high values for the mouse, and perhaps rat, is probably without significance because it is difficult to get a mouse to remain quiet and to measure its pulse rate. The relatively high values for athletic men and animals (horses, dogs, cats) as contrasted to the low values for the non-athletic (beef cattle, "tame rabbits," sheep) is highly significant.

Indices of Work Capacity for Different Species.

Species	Oxygen pulse	Oxygen pulse per kg	Data and source from which the indices at left were computed			
			Body wt. (kg)	Pulse rate per min.	O_2 consumption (cc/min)*	Reference
Mouse, "tame"	0.0024	0.096	0.025	600	1.45	88, 89
Rat, "tame"	.015	.075	.200	440	6.57	88, 89
Guinea pig	.020	.050	.400	267	5.44	89
Rabbit, "tame"	.073	.037	2.0	205	15.0	89
Rabbit	.094	.036	2.6	180	16.9	90
Cat	.230	.092	2.5	122	28.6	89
Marmot	.136	.051	2.6	80	10.9	90
Dog	.52	.080	6.5	120	62.2	89
Dog	.80	.083	9.6	96	76.4	89
Dog	1.44	.072	20	85	122	89
Goat	1.43	.040	36	81	116	90
Goat	1.75	.053	33	135	236	89
Goat, Female	2.98	.060	50	80	238†	91
Sheep	2.15	.048	45	78	168	90
Sheep	2.64	.053	50	75	198	89
Sheep, Male	4.60	.052	88	72	331†	91
Woman	2.74	.049	56	66	181	90
Man	3.95	.061	65	60	237	90
De Mar (athletic)	5.0	.081	61.5	52.1	262†	92
C.V.C. (sedentary)	3.2	.054	59.0	76.6	248†	92
D.B.D. (sedentary)	4.2	.059	71.5	58.2	246†	92
Shetland ponies	22.6	.080	284	42.9	971†	91
Percheron horses	53.1	.082	646	42.8	2271†	91
Beef cow	23.7	.052	457	60	1420†	91
Steer	33.5	.046	730	48	1606	93
Elephant	302.0	.082	3672	31	9377†	94

* Many of the values in this column were computed from metabolism data, Cal/24 hrs., by assuming that 4.8 Calories is the heat equivalent for 1000 cc. of oxygen.

† Non-basal data. Further investigation is needed to study the influence of fasting and other factors on work-capacity indices.

[88] Clark, A. J., "Comparative physiology of the heart," pp. 143–145, The Macmillan Company, New York, 1927.

[89] Cited by Clark.[88]

[90] Benedict, F. G., Carnegie Inst. Wash. Publ., 503, pp. 62, 176, 1938.

[91] Missouri data.

[92] Bock, A. V., Vancaulaert, C., Dill, D. B., Folling, A., and Hurxthal, L. M., *J. Physiol.*, **66,** 136 (1928).

[93] Benedict, F. G., and E. G. Ritzman, Carnegie Inst. Wash. Publ., 377, pp. 226, 227, 1927.

[94] Benedict, F. G., Carnegie Inst. Wash. Publ., 474, pp. 128, 268, 1936.

As previously explained (Sect. 24.5.2), *resting* values of cardio-respiratory capacity may not always be reliable indices of *work* capacity. When we computed[85] our index values for three members of a Yale crew, from *resting* oxygen consumption and pulse rate data reported by Henderson and Haggard,[95] we found values around 0.09 for two of the crew, but only 0.05 to 0.06 for the third, the number 7 crew member. Was the low value for this athlete a normal variation (excitement or slight physical disturbance at the time of the test could have altered the relation between pulse rate and oxygen consumption) or was this number 7 crew member able to compete in thi strenuous sport despite a relatively low index of work capacity by reason of superior "will" to win, coupled perhaps with exceptional ability to go int oxygen debt?*

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[95] Henderson, Y., and Haggard, H. W., *Am. J. Physiol.*, **73,** 193 (1925).

Such a question cannot be answered by a study of *resting* indices; more information may be obtained by a study of the behavior of the index unde *working* conditions.

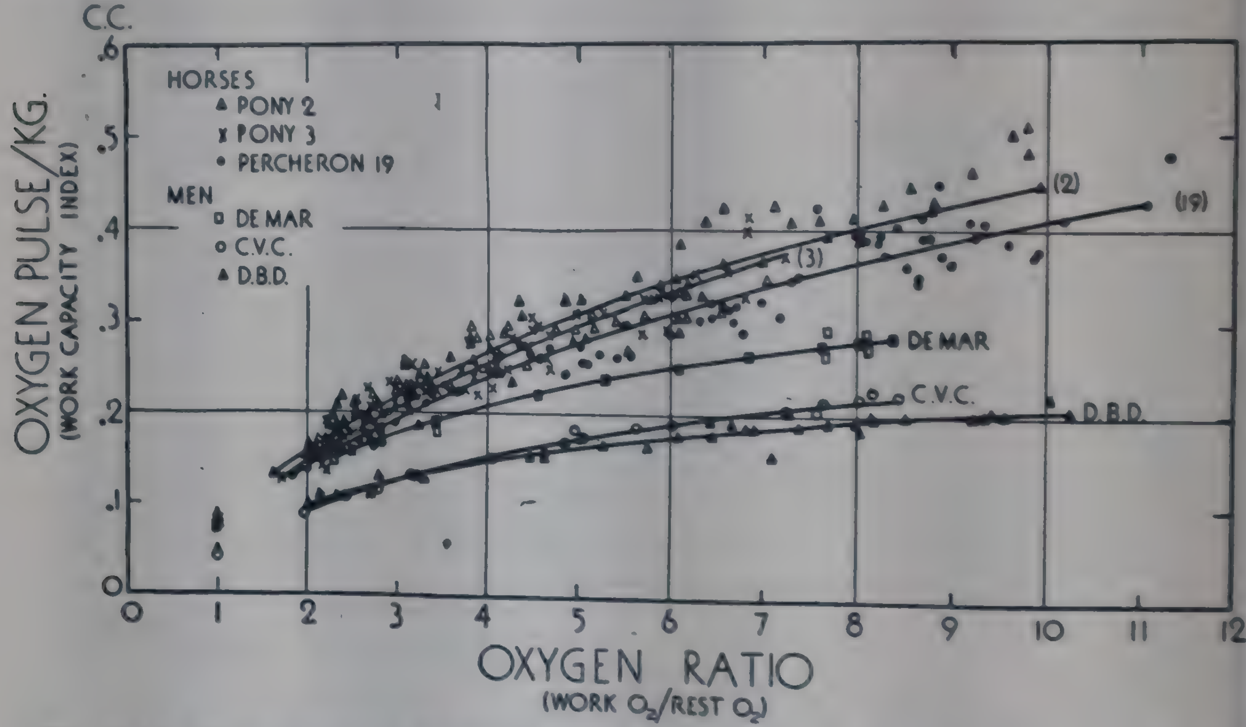

Fig. 24.15. The oxygen-pulse trend with increasing work rate. In order to eliminat differences in body size, the oxygen pulse was divided by body weight and the oxygen consumption rate at given work rates divided by the resting oxygen consumption.

Fig. 24.15, showing curves of oxygen-pulse per kilogram plotted agains oxygen ratio or work level (the ratio of oxygen consumed at a given work leve to that at the resting level) indicates that athletes (De Mar) have a highe oxygen-pulse-weight index at higher work levels than non-athletes (C.V.C and D.B.D.), and that horses have higher oxygen-pulse-weight index value than men. These *work* oxygen-pulse-weight indices are very much mor useful than *rest* oxygen-pulse-weight indices because they discount difference in amibition, temperament, skill, and also physiologically-compensated conditions at lower but not higher work levels. (Attempts to compare oxyge pulse without correcting for differences in body size and differences in resting oxygen consumption were not successful, as illustrated in Fig. 24.16a.)

Summarizing this section, muscular exercise calls for the integrated actio of many functions, any one of which may become limiting in the work capacit complex. On the other hand, serious faults may be compensated or maske by various mechanisms; this explains occasional break-downs of great athlete in their apparent prime. There can, therefore, be no infallible measure o vork capacity. Maximal oxygen consumption, maximum pulmonary venilation, rapidity of functional adjustment from rest to work and from work o rest are good capacity indices. Special consideration is given to the oxygen onsumption per heart beat per unit weight (oxygen pulse per unit weight) s index of work capacity applicable to other species as well as man, *regardless of body weight.* The rational (mathematical) aspects of this index are discussed in detail, and it is shown that the basal metabolism of mature animals of different species is directly proportional to the product of body weight and the basal pulse rate.

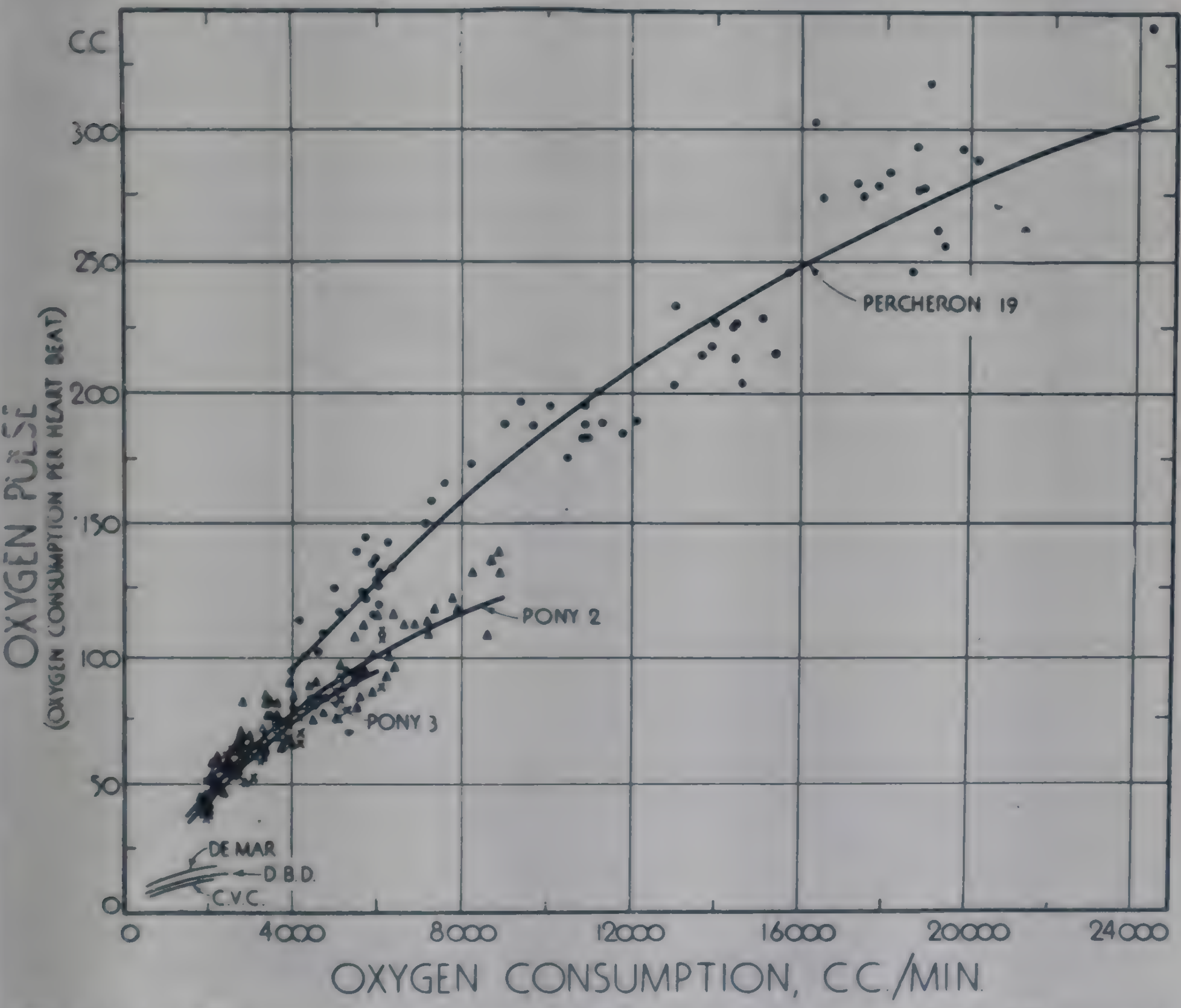

Fig. 24.16a. If the oxygen pulse and metabolism are not corrected for differences in body size, the curves are not comparable as here shown. Hence the corrections in ig. 24.15.

24.6: Relative economy of horse and tractor. The maximum gross energetic efficiency of muscular work in animals, 25 per cent, is at least as great s of tractors (13–19 per cent for ignition and 22–26 per cent for Diesel-type ngines). Animals, however, must rest, and all day energetic efficiency and nonetary economy vary with the number of working hours (Figs. 24.10a o e). Table 24.3a shows that per horse-power hour, the feed cost is 2.14 ents when the horse works 12 hours a day, 3.5 cents when he works 4 hours a day, and 5.5 cents when he works 2 hours a day. On the other hand, while the engine does not consume fuel when at rest, the depreciation and interest charges are greater than for the animal, and the working hours per year are fewer for the tractor than for the horse. Tables 24.3b and c from Smith and Jones[96] support our data in Table 24.3a.

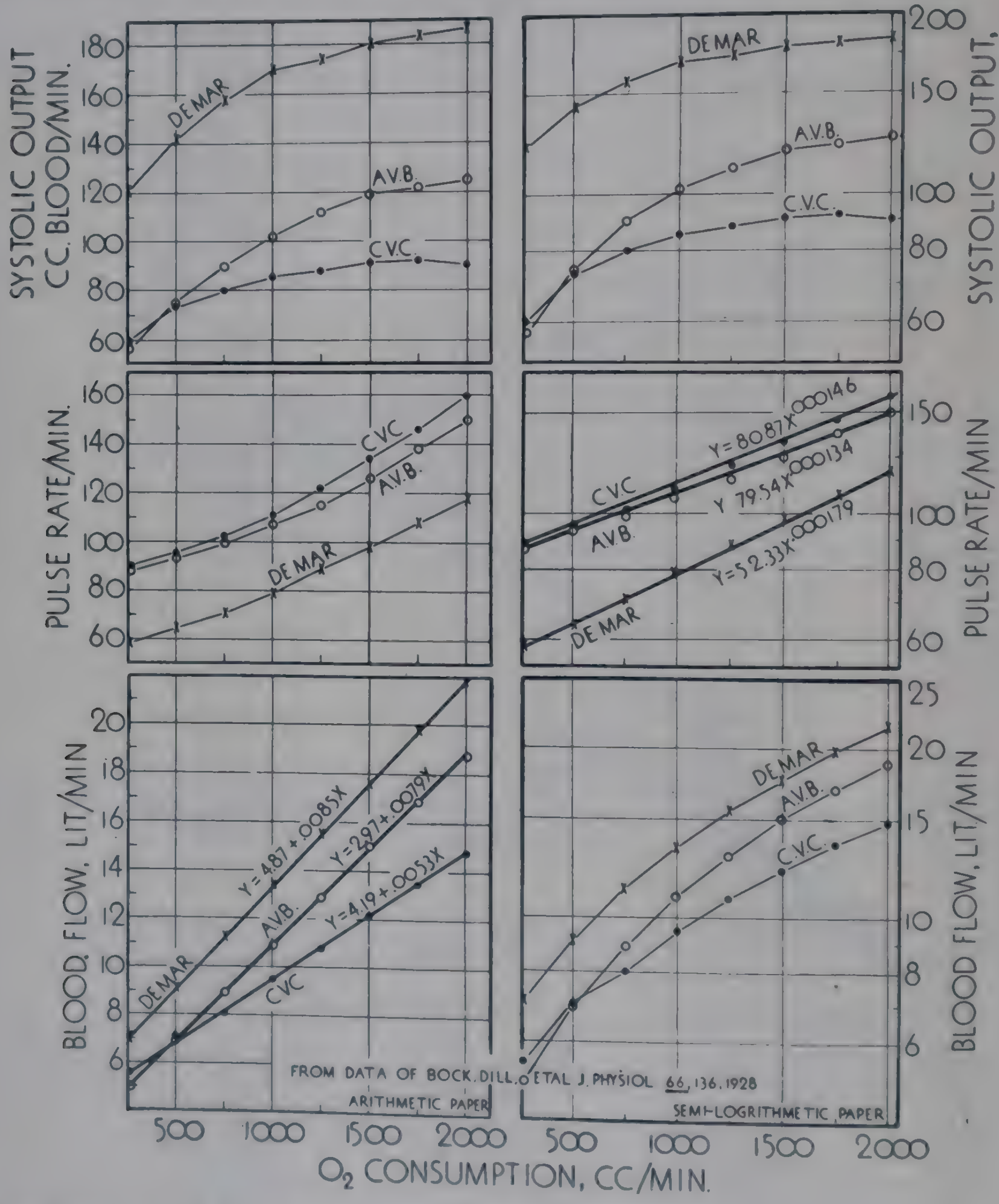

Fig. 24.16b. Blood flow, pulse rate, and systolic output as function of work rate (O consumption).

Comparison between all-day monetary economy of horses and tractors is difficult because of the instability of relative price per unit of tractor and horse fuels. Thus if it is assumed that a pound *TDN* costs 1 cent and contains 2000 Calories, and a gallon kerosene costs 10 cents and contains 41,000

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[96] Smith, D. D., and Jones, M. M., "Power, labor and machine costs in crop production." Univ. Mo. Agr. Exp. Sta. Res. Bull. 197, 1933.

Calories, then *per* 1000 *Calories*, *TDN* costs ½ cent and kerosene costs ¼ cent. But feed and gasoline prices vary and overhead investments for horses and tractors vary. There are, moreover, many considerations which do not lend themselves to quantitative comparisons, such as income for young stock, utilization of pastures and other feed sources which might otherwise be wasted, superior adaptability of horse, consideration of initial investment with its associated interest payments, smallness of farm for a 12 H.P. tractor, "keeping the money on the farm" and so on. Table 24.3 presents estimates of efficiencies, energy costs, and hypothetical monetary costs and overhead expenses of horse and tractor as far as they can be tabulated, leaving the reader to compare other factors which fluctuate with our rapidly changing economic frame-work.

24.7: Summary. This chapters covers a rather broad territory: the place of the horse in our national economy; the energetic efficiency of the horse in in comparison to machines; work levels; energetic cost of muscular work; limiting factor in work capacity; measures of work capacity; relative monetary economy of horses and tractors on the farm. The sections on each of these topics were separately summarized from which the following comments are abstracted.

The maximal gross energetic *efficiency* of muscular work is close to 25 per cent in both 1500-lb horses and 150-lb men: of 100 Calories energy expended (of fuel oxidized in the body during work) not over 25 Calories can be recovered in work accomplished. This 25 per cent maximum efficiency level is approached exponentially with increasing work rate, in accordance with the law of diminishing returns.

The gross[97] and net[97] costs of work increase linearly with increasing speed, load, and horse power. The gross and net costs per unit work, or per unit power, decrease hyperbolically with increasing power (Fig. 1.4). But the absolute energy cost is nearly independent of rate of work; it is of the order of 1000 Calories per mega foot-pound (million foot-pounds); or 2000 Calories per horse power-hour (Fig. 1.4). The decline of gross and net cost per unit work with increasing work rate is hyperbolic, the asymptote of which is the absolute-cost curve (Fig. 1.4). The reason for this decline of cost per unit work with increasing work rate is that the higher the work rate the smaller the fraction of total energy expense that goes for maintenance or for mere walking without a load. When the work-rate is very great, the overhead maintenance expense becomes negligible by comparison with total energy expense so that the *gross* and *net* costs per unit work become almost identical

[97] *Gross* energy cost includes resting maintenance; *net* energy cost does not include resting maintenance cost *absolute* energy costs does not include cost of walking without load. *Gross efficiency* is the ratio of work-energy accomplished to total energy expended; *net efficiency* is the ratio of work energy accomplished to energy expended above that at rest; *absolute efficiency* is the ratio of work energy accomplished to energy expended.

with *absolute* cost; that is, gross and net costs per unit work approach asymptotically the absolute cost. The analysis of the work data on the horses is compared with the results of thermodynamic theory (see also Chs. 2 and 3).

An analysis is presented of relative metabolism at various levels of effort and the influence of body size thereon. The ratio of maximal to minimal *oxygen consumption* is of the same order in horses and men, namely about 20; the ratio of maximal to minimal *energy expenditure* is of the same order in horses and men, namely about 100; the ratio of energy expenditure during sustained heavy work 8 hours a day, as encountered in daily life, to basal metabolism, is of the same order in horses and men, namely about 8.

Mechanisms limiting work capacity are discussed with special reference to blood circulation, pulmonary ventilation, oxygen-carrying capacity of blood, ability to incur oxygen debt, capacity of the coronary circulation, body-temperature regulation, nutritional and hormonal factors.

Methods of measuring work capacity are discussed critically with special reference to maximal oxygen consumption, maximum pulmonary ventilation, metabolic-adjustment rates. Special attention is given to oxygen consumption per heart beat per unit weight (oxygen pulse per unit weight) as index of work capacity.

The chapter closes with a brief discussion of the relative economy of horses and tractors followed by an appendix on tabular data, alignment charts, and supplementary charts.

24.8: Appendix.

24.8.1—Equations for energy cost of muscular work and for gross or overall energetic efficiency. If speed differences are disregarded, the relation of gross or overall energy expended, Q_o, to horse-power, H.P., is, for Horse 19,

$$Q_o = 1065 + 2339 \text{ H.P.} \qquad (1)$$

If, however, the data are separated by speeds, then small but definite differences are found as shown by the following equations (upper half of Fig. 24.6a).

Liters oxygen per minute *Calories per hour*

$$O_2 = 3.54 + 7.27 \text{ (H.P.)} \quad Q_o = 1062 + 2181 \text{ H.P.} \quad \text{Speed} = 1.15 \text{ m/hr} \qquad (2)$$

$$O_2 = 4.03 + 7.47 \text{ (H.P.)} \quad Q_o = 1209 + 2241 \text{ H.P.} \quad \text{Speed} = 2.2 \text{ m/hr} \qquad (3)$$

$$O_2 = 4.79 + 7.41 \text{ (H.P.)} \quad Q_o = 1437 + 2223 \text{ H.P.} \quad \text{Speed} = 3.1 \text{ m/hr} \qquad (4)$$

The gross or overall efficiency, E_o, of the work may be computed from the above equations and from the equivalence of 1 H.P. and 642 Cal/hr (lower half of Fig. 24.6a).

$$E_o = \text{Gross or overall efficiency} = \frac{\text{(H.P.) } 642}{Q_o} \qquad (5)$$

Substituting equations (1), (2), (3), and (4) in equation (5) separately, gives the equations for efficiency at speeds 1.15, 2.2, and 3.1 miles per hour. All these equations pass through zero-zero and approach asymptotically the maximum efficiency value.

Thus substituting eq. (1) in (5),

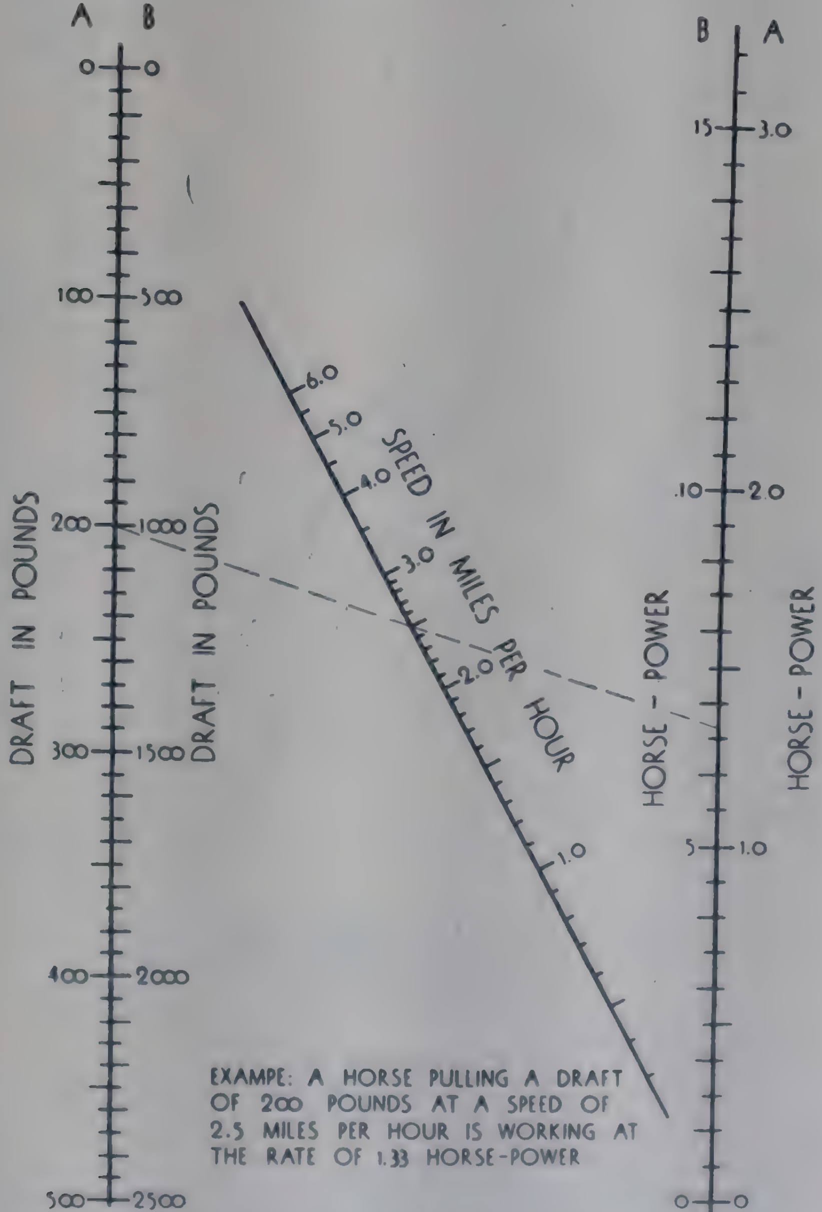
$$E_o = \frac{(\text{H.P.})\ 642}{1065 + 2339\ \text{H.P.}} \times 100 \tag{6}$$

Dividing numerator and denominator by H.P.,

$$E_o = \frac{64200}{\dfrac{1065}{\text{H.P.}} + 2339} \tag{7}$$

The limiting value of efficiency becomes:

$$E_o = \frac{64200}{\dfrac{1065}{\alpha} + 2339} = \frac{64200}{2339} = 27.4\% \tag{8}$$



EXAMPE: A HORSE PULLING A DRAFT OF 200 POUNDS AT A SPEED OF 2.5 MILES PER HOUR IS WORKING AT THE RATE OF 1.33 HORSE-POWER

Fig. 24.17. Alignment chart for estimating horse power from draft (tractive pull) and speed. Thus to convert a 200-pound draft pulled at 2.5 miles per hour into horse-power stretch a string between 200 on the left scale and 2.5 on the middle scale and read the answer (1.33 horse-power) on right scale.

Similarly for equations (2), (3), and (4) the maximum efficiencies are:

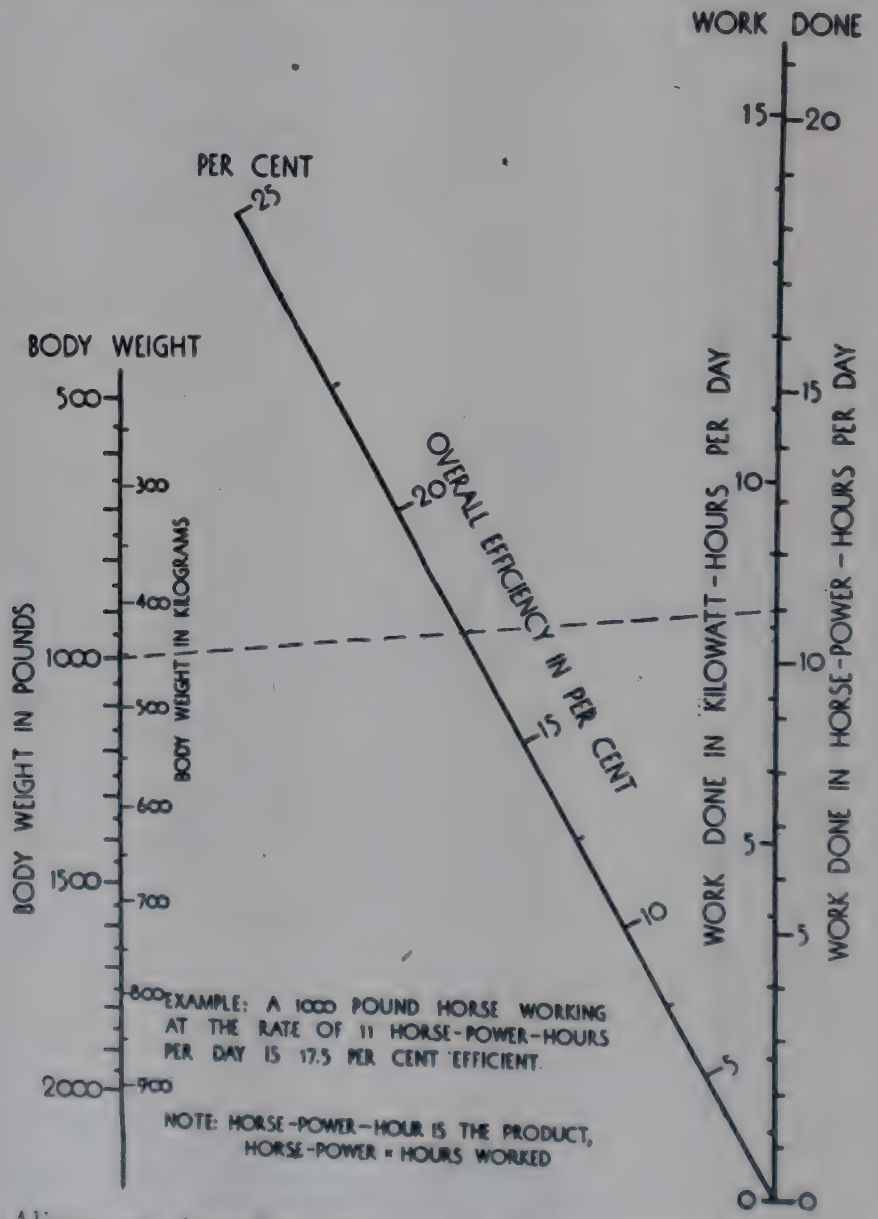
$$29.4\% \text{ for speed } 1.15 \text{ mph} \tag{9}$$

$$28.6\% \text{ for speed } 2.2 \text{ mph} \tag{10}$$

$$28.8\% \text{ for speed } 3.1 \text{ mph} \tag{11}$$

These gross maximal efficiency values are evidently too high after we said that the maximal gross efficiency cannot exceed 25 per cent.

The problem of maximum efficiency may be approached from another point of view. The course of efficiency with increasing horse-power resembles the age curve of growth in weight represented by the equation $Y = A - Be^{-kx}$. This exponential equation was therefore fitted to the data by rectification on semi-log paper, as outlined in Ch. 16



EXAMPLE: A 1000 POUND HORSE WORKING AT THE RATE OF 11 HORSE-POWER-HOURS PER DAY IS 17.5 PER CENT EFFICIENT.

NOTE: HORSE-POWER-HOUR IS THE PRODUCT, HORSE-POWER × HOURS WORKED

Fig. 24.18. Alignment chart for estimating overall, or gross, energetic efficiency (on basis of 24-day maintenance) from body weight of horse and amount of work accomplished per day. Thus, if it is desirable to find the gross energetic efficiency of a 1000-pound horse working at the rate of 11 horse-power-hours per day, stretch a string between 1000 on left scale and 11 on the right scale and read the answer, 17.5 per cent, on the middle scale.

with the following results:

$$E_o = 25.0\ (1-e^{-1.79\ \text{H.P.}}) \qquad \text{Speed} = 1.15 \text{ mph} \qquad (12)$$

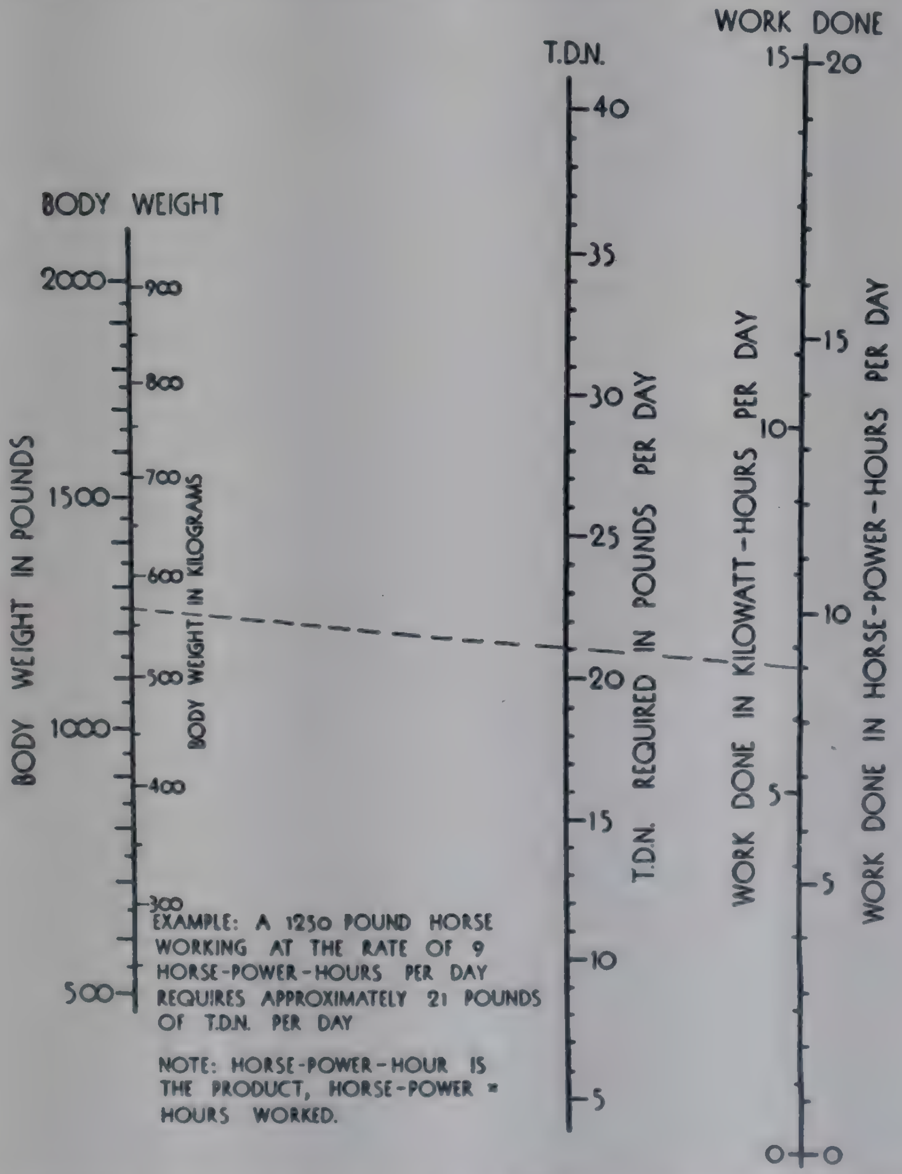
$$E_o = 24.5\ (1-e^{-1.41\ \text{H.P.}}) \qquad \text{Speed} = 2.2 \text{ mph} \qquad (13)$$

$$E_o = 24.0\ (1-e^{-1.20\ \text{H.P.}}) \qquad \text{Speed} = 3.1 \text{ mph} \qquad (14)$$

The resulting curves and the accuracy of the fit are shown in the lower half of Fig. 24.6a, and are entirely reasonable.

It may be noticed that equation (7) more nearly represents the data in the region from about 0 to 0.75 H.P. than equations (12), (13), and (14). On the other hand, (12), (13), and (14) more nearly represent the data from about 0.75 to 2 H.P. Above 2 H.P. there is little difference within the range of the data.

The exponential-equation method (12, 13, 14) appears to be better suited for relating the course of overall efficiency with increasing horse-power than the "rational" sub-

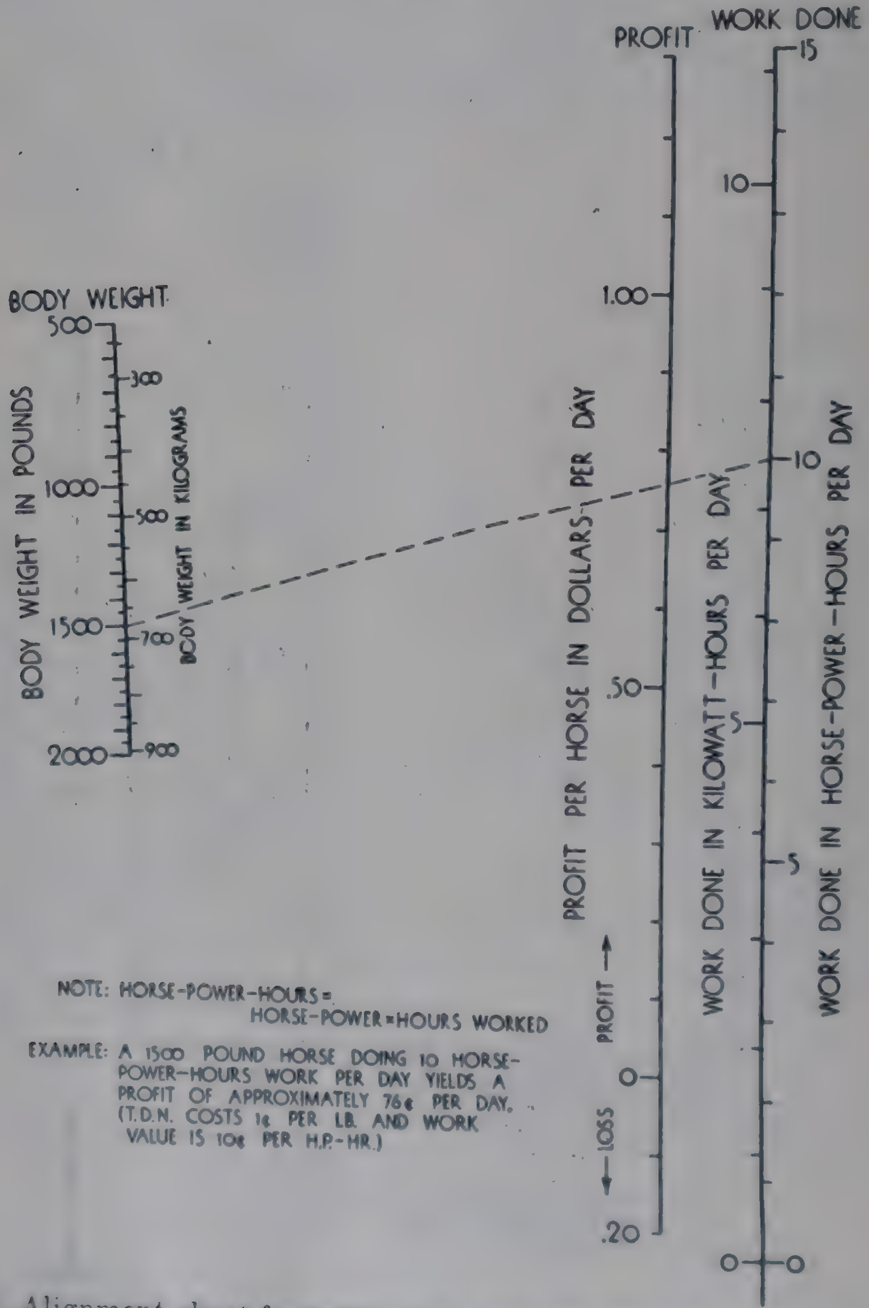


EXAMPLE: A 1250 POUND HORSE WORKING AT THE RATE OF 9 HORSE-POWER-HOURS PER DAY REQUIRES APPROXIMATELY 21 POUNDS OF T.D.N. PER DAY

NOTE: HORSE-POWER-HOUR IS THE PRODUCT, HORSE-POWER × HOURS WORKED.

Fig. 24.19. Alignment chart for estimating feed (TDN requirements) from body weight of horse and work accomplished. To find TDN required by a 1250-pound horse working at the rate of 9 horse-power-hours per day, stretch a string between 1250 on left scale and 9 on right scale and read the answer, 21 pounds TDN, on the middle scale.

stitution method (6, 7, 9, 10, 11), first, because the substitution method is based on the assumption that the energy expense is a linear function of horse-power. This assumption probably does not hold for higher horse-powers (see Fig. 24.3). The exponential equation, on the other hand, is frankly empirical, used with the full understanding that efficiency goes through a maximum, after which it declines rapidly with increasing horse-power. In other words, there is an implicit limitation against the use of the exponential equation beyond a certain value. Moreover, the maxima overall efficiency values obtained by the exponential-equation method (24 per cent to 25 per cent) appear to be more reasonable than the maxima derived by the substitution method (28 per cent



NOTE: HORSE-POWER-HOURS = HORSE-POWER × HOURS WORKED

EXAMPLE: A 1500 POUND HORSE DOING 10 HORSE-POWER-HOURS WORK PER DAY YIELDS A PROFIT OF APPROXIMATELY 76¢ PER DAY. (T.D.N. COSTS 1¢ PER LB. AND WORK VALUE IS 10¢ PER H.P.-HR.)

Fig. 24.20. Alignment chart for estimating profit or loss on horse at given work price (10 cents per horse power), and given feed price ($1.00 per 100 pounds TDN) from body weight of horse and work accomplished per day.

to 29 per cent). Finally, the exponential equation fits[98] the data better in the 1 H.P. region, which represents the "standard" power output of a horse.

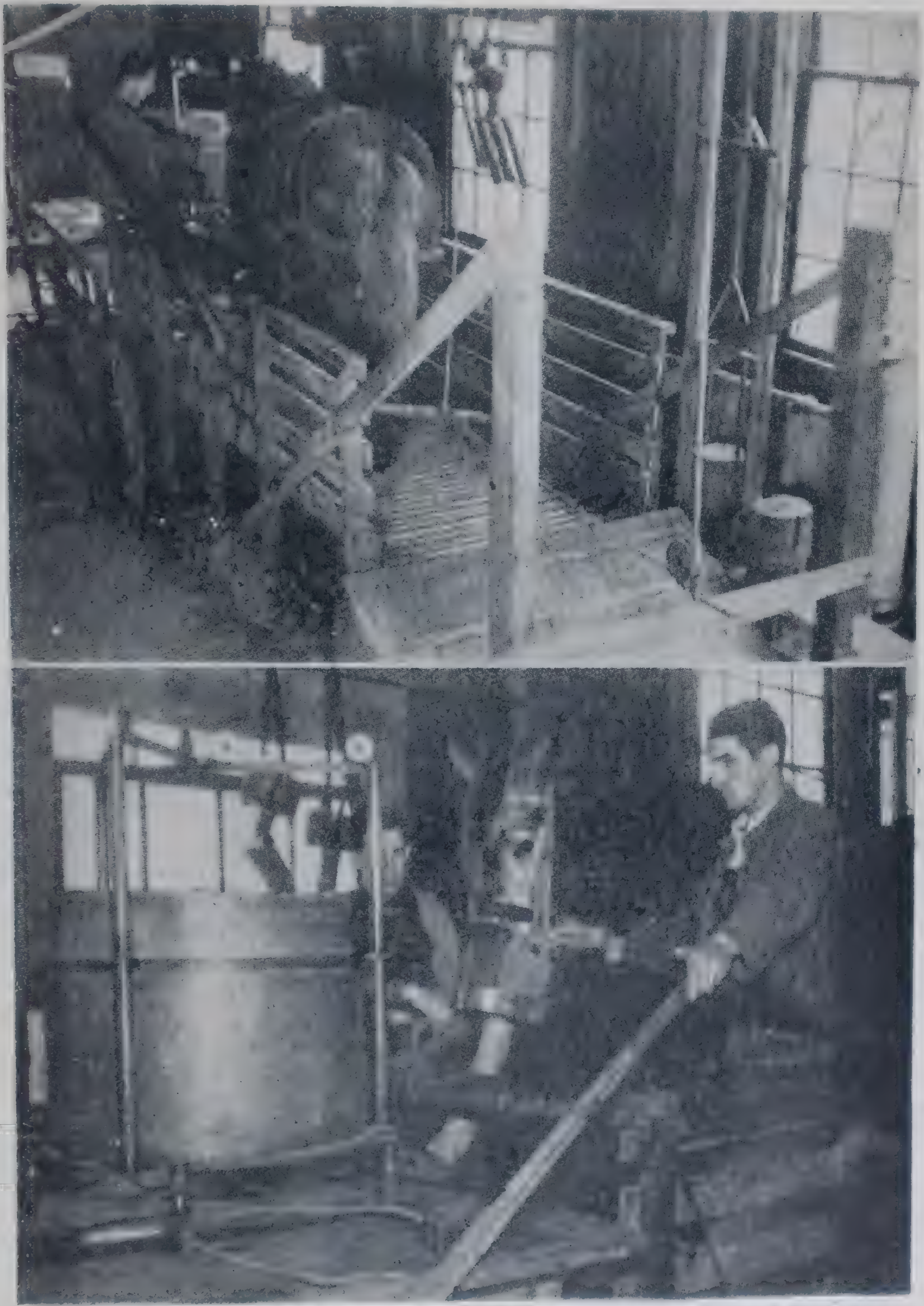


Fig. 24.21. Photograph of our treadmill-metabolism apparatus (cf. Fig 24.1).

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[98] The irregularities of the data are due largely to the fact that they were secured at varying intervals, in one case 7 months apart, when the horses were in widely varying physical conditions and body weights. The 1500-pound horse worked on an outlying farm a considerable distance from the laboratory, and could rarely be spared for measurements; the pony likewise worked in a mine some distance away.

In connection with the discussion of relative reasonableness of 24 per cent to 25 per cent and 28 per cent to 29 per cent as gross efficiency maxima, it may be noted that the "absolute efficiency" (equation 3.3) is the theoretical maximal limit of gross and net efficiency. The absolute efficiency represented by the bottom curve of Fig. 1.4 (end of Ch. 1) is of the order of 30 per cent; therefore, gross and net, efficiency can never reach 30 per cent, but approach 30 per cent as a limit, 28 per cent to 29 per cent is too close to the maximum to be reasonable.

As regards the influence of the number of hours worked per day on efficiency and profit, all-day work efficiency is, of course, much below working-hour efficiency, and it varies with the number of working hours as illustrated in Fig. 24.10 and the following equations.

The equation for all-day efficiency, as function of hours worked per day may be derived from equation (1) and from the energy expended during standing. If N is number of hours worked, and 607 Cal are expended per hour while standing at rest,

Fig. 24.22. Photograph of the Kaiser-Wilhelm Institute for the physiology of work, Dortmund, Germany (1931).

then the all-day energy expended, Q_o, is

$$Q_o = (24 - N)\,607 + N\,(1065 + 2339 \text{ H.P.}) \tag{15}$$

The calorie equivalent of the work accomplished is

$$Q_{wa} = 642 \times \text{H.P.} \times N \tag{16}$$

The gross or overall efficiency, E_o, is then,

$$E_o = \frac{Q_{wa}}{Q_o} = \frac{642 \text{ H.P.} \times N}{(24 - N)\,607 + N\,(1065 + 2339 \text{ H.P.})} \tag{17}$$

This equation may be simplified by assuming the horse to work at the rate of one horse-power and collecting terms, giving,

$$E_o = \frac{642\,N}{14570 + 2793\,N},$$

which is the equation of the curve of Fig. 24.10c (right side).

The variation of profit with hours worked per day (left side of above Fig.) gives a different picture. We may assume the value of work accomplished to be 10¢ per horse-power-hour and the cost of the feed 1¢ per lb *TDN*. Since 1 horse-power-hour is equivalent to 642 Cal and 1 lb *TDN* to 1814 Cal, we have $\frac{.10}{642}$ dollar per Cal of work accomplished, and $\frac{.01}{1814}$ dollar per Cal of energy expended. Thus, referring to equations 15 and 16, the equation for profit (the value of work accomplished minus the cost of feed required) may be written

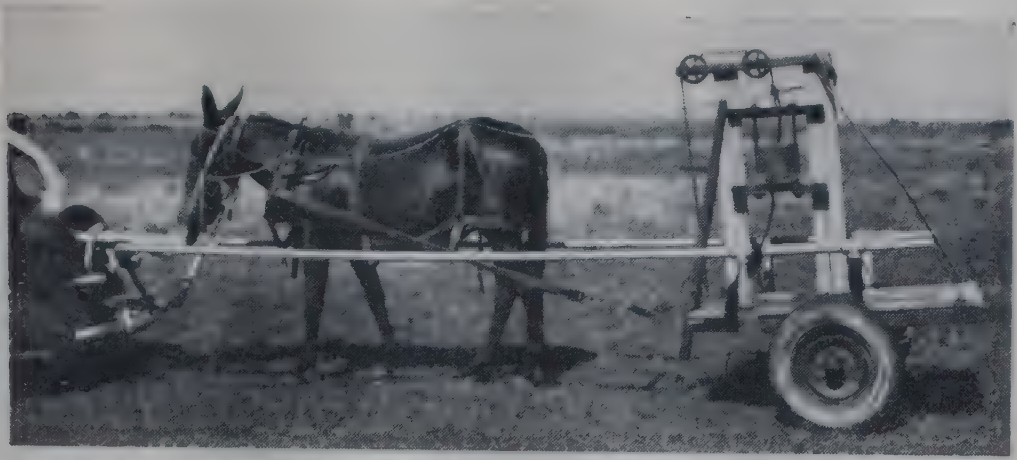

Fig. 24.23a. Photograph of our field-work-metabolism apparatus. The trailer on which the weight ergometer is mounted is pulled by the car at the desired speed and the mule pulls the given ergometer weight at the speed set by the car. The respiratory system of the animal is connected by a mask to gas meter and aliquoting apparatus within the car. This apparatus was built by James Sappington under the early direction of C. W. Winchester and later direction of H. H. Kibler, who will report in a joint monograph from the U. S. Dept. of Agriculture and the Univ. Missouri Agr. Exp. Sta. within the year on its details and experimental results obtained therewith.

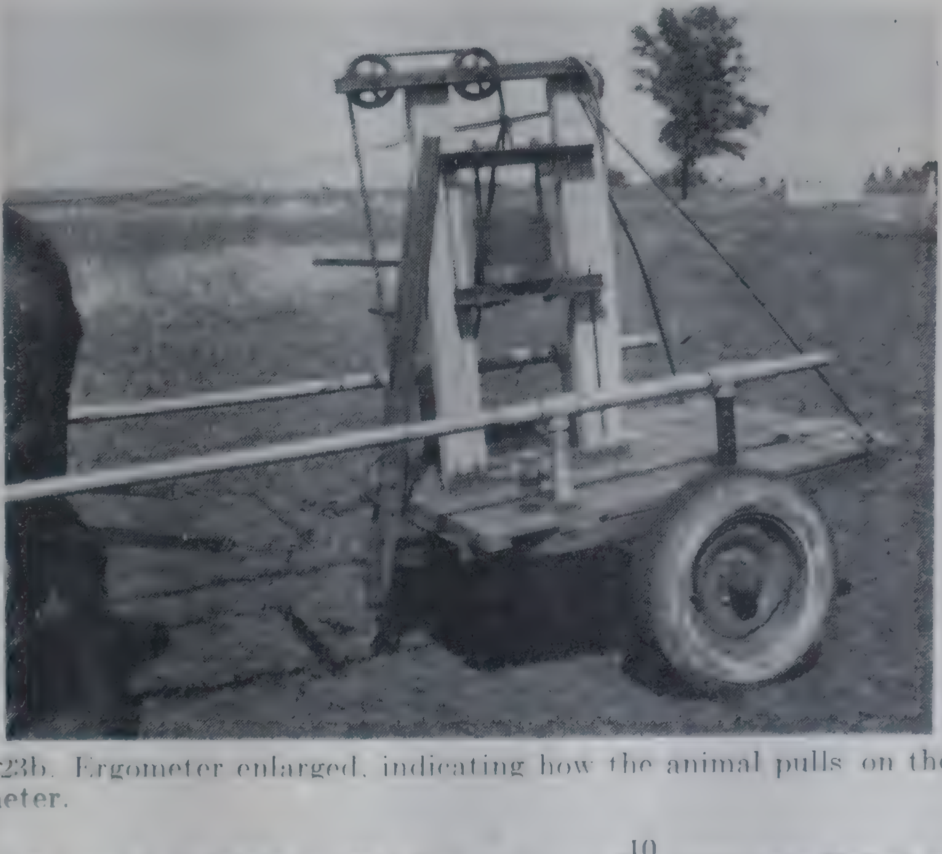

Fig. 24.23b. Ergometer enlarged, indicating how the animal pulls on the weight in the ergometer.

$$\text{Profit} = \frac{.10}{642} Q_{wa} - \frac{.01}{1814} Q_o \tag{18}$$

$$= \left\{\frac{.10}{642} \times 642 \times \text{H.P.} \times N\right\} - \left\{\frac{.01}{1814} [(24 - N)\, 607 + N\, (1065 + 2339\ \text{H.P.})]\right\} \tag{19}$$

For a work rate of one-horse this equation reduces to

$$\text{Profit} = .10N - .01\, \frac{14570 + 2793N}{1814} = -.0803 + .0846N \tag{20}$$

The above equation indicates that, unlike efficiency, profit is *linearly related* to the number of hours worked.

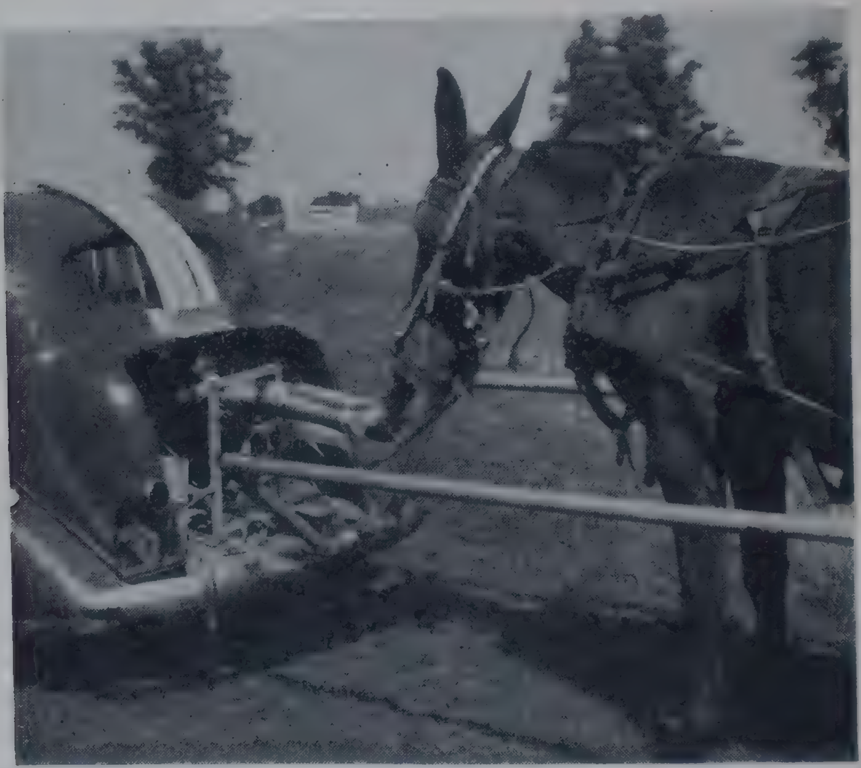

Fig. 24.23c. The connection of the animal's muzzle to the gas meter.

In brief, as shown in Fig. 24.10c, the increases in all-day efficiency (a ratio) with increasing number of hours worked per day decreases; but the increase in profit (a difference) per day is constant; that is, the profit increments per day per animal increase linearly with the number of hours worked per day, but the efficiency increment decreases exponentially with increasing work hours per day.

24.8.2: Alignment charts. Some of the above aspects may be represented as alignment charts or nomographs (for methods of construction see Univ. Missouri Agr. Res. Bull. 239, 1936.

Relation between load, speed, and horse power. Fig. 24.17 shows this relation. Thus, if it is desired to find the horse-power developed when a 200-lb draft is pulled at the rate of 2.5 miles an hour, a straight edge is placed (or a string is stretched) across the chart between points 200 on the draft scale and 2.5 on the speed scale, and the answer, 1.33 horse-power, is read on the horse-power scale. Draft values on scale A, of course, refer to horse-power values on scale A, and draft values on scale B refer to horse-power values on scale B. Similar technique is used in the other charts.

This nomograph was constructed from the relation

$$\text{H.P.} = D \times \frac{5280}{1980000} \times S = D \times 0.002667S \tag{21}$$

(D = draft or load in pounds; S = speed in miles per hour)

Letting, H.P. = Z, $D = X$, and $.002667S = Y$, equation (15) becomes

$$Z = X \cdot Y \tag{22}$$

which, is the general equation of a Z type nomograph (Univ. Missouri Agr. Res. Bull. 239, 1936).

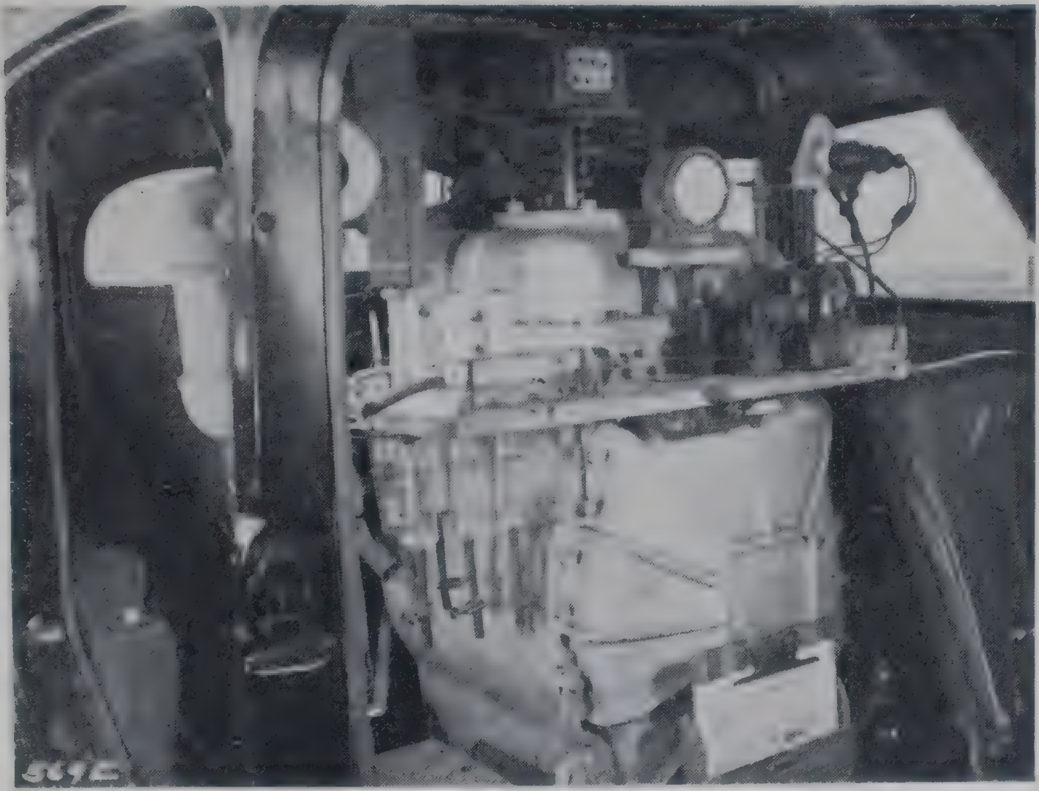

Fig. 24.23d. Gas meter within the car and the aliquoting sampling tubes.

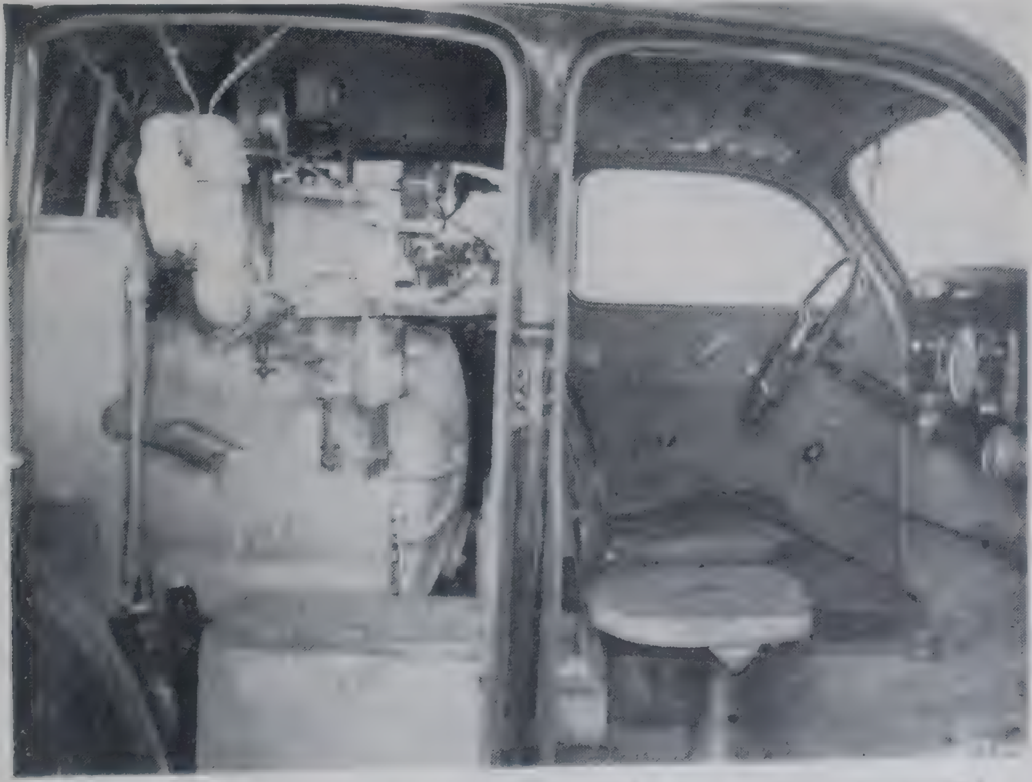

Fig. 24.23e. Sideview of the interior of the car and its equipment

Relation between body weight, work accomplished, and overall or gross efficiency. This is shown in Fig. 24.18. Example: A 1000-lb horse performing 100 horse-power-hours of work per day (24 hours) has an all-day (including resting time) mechanical efficiency of 17½ per cent (answer obtained on efficiency scale by stretching string between 1000 on body-weight scale and 11 on horse-power-hour scale).

Fig. 24.18 is based on the *TDN* partition equation (Ch. 21).

$$TDN = 0.053M^{0.73} + 1.27 \text{ H.P.-hr} \tag{23}$$

in which the maintenance term is assumed equal to that found for cows (Ch. 21), $0.053M^{0.73}$. The work term, 1.27 H.P.-hr, is derived from the linear relation of Q_o to H.P. (equation 1 in which it is seen that 2300 Cal/hr are expended per H.P. above a constant for maintenance).

By definition, the gross or overall efficiency is

$$E_o = k\,\frac{\text{H.P.-hr}}{TDN}\,\% \tag{24}$$

where k is a factor for converting the work and feed to the same units, and multiplying by 100 for percentage. If *TDN* is expressed in pounds (1 lb *TDN* = 1814 Cal), $k = 35.34$. Substituting equation (23) in (24) gives,

$$E_o = \frac{35.34 \text{ H.P.-hr}}{.053M^{0.73} + 1.27 \text{ H.P.-hr}} \tag{25}$$

Taking the reciprocals

$$\frac{1}{E_o} = \frac{.053M^{0.73}}{35.34 \text{ H.P.-hr}} + \frac{1.27 \text{ H.P.-hr}}{35.34 \text{ H.P.-hr}} \tag{26}$$

or

$$\frac{1}{E_o} = \frac{.001500M^{0.73}}{\text{H.P.-hr}} + 0.03594 \tag{27}$$

Let $.001500M^{0.73} = X$, $\dfrac{1}{\text{H.P.-hr}} = Y$, and $\left(\dfrac{1}{E_o} - .03594\right) = Z$, then equation (27) becomes,

$$Z = X \cdot Y \tag{28}$$

which is the general equation of the Z type chart (Univ. Missouri Agr. Exp. Sta. Res. Bull. 239, 1936).

Feed standard: Feed (TDN) needs for different body weights and work rates. Fig. 24.19 represents the relation between body weight of horse, work accomplished per day (of 24 hours), and feed in the form of *TDN* required per day (of 24 hours). Thus a 1250 lb horse working at the rate of 9 horse-power-hours of work per day needs about 21 lb *TDN* per day. Fig. 24.19 is supplemented by Tables 24.3c and d.

Fig. 24.19 is merely an adaptation of equation (23) to an alignment chart. By letting $TDN = Z$, $0.053M^{0.73} = X$; and $1.27 \text{ H.P.-hr} = Y$, equation (23) may be rewritten

$$Z = X + Y \tag{29}$$

which is the general equation of the parallel line chart (Univ. Missouri Agr. Exp. Sta. Res. Bull. 239, 1936).

Profit for given work rates by horses of different body weight, represented in Fig. 24.20, was constructed on the assumption that feed for horses costs 1 cent per pound *TDN*, and work power sells at 10 cents per horse-power-hour. Work is estimated, with the aid of Fig. 24.17, from the load pulled and the speed with which it was pulled.

By profit we mean value of work less cost of feed. Assume the cost of feed to be \$1.00 per 100 lb *TDN*, and the value of the work done, 10 cents per horse-power-hour (\$1.00 per day for a 10 H.P.-hour day).

$$\text{Profit} = 0.10\ \text{H.P.-hr} - 0.01\ TDN \tag{30}$$

Substituting equation (23) in (30) gives,

$$\text{Profit} = 0.10\ \text{H.P.-hr} - 0.01\ (.053M^{0.73} + 1.27\ \text{H.P.-hr}) \tag{31}$$

or

$$\text{Profit} = 0.0873\ (\text{H.P.-hr}) - 0.00053M^{0.73} \tag{32}$$

Let $(-0.00053M^{0.73}) = X$, 0.0873 H.P.-hr $= Y$, and Profit $= Z$, then equation (31) becomes

$$Z = X + Y \tag{33}$$

which is the general equation of the parallel line chart (Univ. Missouri Agr. Exp. Sta. Res. Bull. 239, 1936).

Table 24.1. Data for Shetland Ponies and Percheron Colt.

Expt.	Draft (lbs)	Energy Output (Cal/hr)		Energy Expense (Cal/hr)			Efficiency of Work (%)			Cardiorespiratory Activities				Ratios			Room Temp. (°C)
		$Q_{w.a}$ (Work accomplished)	H.P. (Horse-Power)	Q_o (Overall energy)	Q_n (Net energy)	Q_a (Absolute energy)	O.E. (Overall efficiency)	N.E. (Net efficiency)	A.E. (Absolute efficiency)	Pulse (rate per min)	Respiration (rate per min)	Tidal Air (liters)	Ventilation rate (liters per min)	$\frac{\text{H.P.}}{\text{M lbs.}}$ (M = wt. of horse)	$\frac{\text{Draft}}{\text{M lbs.}}$	Q_o/Q_s	
(A) Shetland Pony No. 2 ♀. Age 4 years. Weight 586 lbs. (266 kgs.). Walking at 1:15 miles per hour (30.85 meters per minute).																	
Standing	0	—	—	241	—	—	—	—	—	40.3	14.7	5.50	81	—	—	1.00	17
Walking	0	—	—	527	286	—	—	—	—	43.4	21.5	5.67	122	—	—	2.19	16
Working	25	49	0.08	659	418	132	7.4	11.7	37.1	46.4	24.0	6.00	144	.000137	.043	2.73	14
Working	50	98	0.15	820	579	293	12.0	16.9	33.4	46.4	28.4	6.06	172	.000256	.085	3.41	14
Working	75	147	0.23	927	686	400	15.9	21.4	36.8	49.2	33.7	5.90	199	.000392	.128	3.85	14
Working	100	197	0.31	1056	815	529	18.7	24.2	37.2	51.2	36.1	6.26	226	.000529	.171	4.38	16
Working	125	246	0.38	1283	1042	756	19.2	23.6	32.5	57.2	40.7	6.96	283	.000648	.213	5.32	17
Working	150	295	0.46	1518	1277	991	19.4	23.1	29.8	60.0	38.7	7.32	283	.000785	.256	6.30	20
Working	175	344	0.54	1575	1334	1048	21.8	25.8	32.8	60.4	44.6	7.44	332	.000921	.299	6.54	20
(B) Shetland Pony No 2 ♀. Age 4 years. Weight 600 lbs. (272 kg). Walking at 2.2 miles per hour (59.00 meters per minute)																	
Standing	0	—	—	261	—	—	—	—	—	39.4	12.6	5.21	65	—	—	1.00	16
Walking	0	—	—	637	376	—	—	—	—	43.4	20.9	5.64	118	—	—	2.44	16
Working	25	94	0.15	839	578	202	11.2	16.3	46.5	46.1	27.5	5.63	155	.000250	.042	3.21	16
Working	50	188	0.29	1073	812	436	17.5	23.2	43.1	50.2	33.5	5.96	200	.000483	.083	4.11	17
Working	75	282	0.44	1362	1101	725	20.7	25.6	38.9	53.9	40.2	5.97	240	.000733	.125	5.22	17
Working	100	376	0.59	1665	1404	1028	22.6	26.8	36.6	61.3	42.2	6.58	278	.000983	.167	6.38	17
Working	175	470	0.73	2092	1831	1455	22.5	25.7	32.3	60.7	41.9	7.60	319	.001217	.208	8.02	15
Working	150	564	0.88	2533	2272	1896	22.3	24.8	29.7	69.8	46.5	7.82	364	.001467	.250	9.71	15
(C) Shetland Pony No. 3 ♂. Age 2 years. Weight 614 lbs. (279 kgs). Walking at 1.15 miles per hour (30.85 meters per minute).																	
Standing	0	—	—	257	—	—	—	—	—	42.9	16.8	5.23	88	—	—	1.00	13
Walking	0	—	—	469	212	—	—	—	—	43.3	23.1	4.98	115	—	—	1.82	14
Working	25	49	0.08	632	375	163	7.8	13.1	30.1	46.5	30.5	4.91	150	.000130	.041	2.46	13
Working	50	98	0.15	769	512	300	12.7	19.1	32.7	49.4	31.2	5.22	163	.000244	.081	2.99	15
Working	75	147	0.23	880	623	411	16.7	23.6	35.8	48.6	36.1	5.10	184	.000374	.122	3.42	15
Working	100	197	0.31	1070	813	601	18.4	24.2	32.8	57.7	39.6	5.65	224	.000505	.163	4.16	15
Working	125	246	0.38	1211	954	742	20.3	25.8	33.2	58.3	42.6	5.78	246	.000619	.204	4.71	15
Working	150	295	0.46	1499	1242	1030	19.7	23.8	28.6	64.7	40.0	6.72	269	.000749	.244	5.83	17

Table 24.1.—*Continued.*

Expt.	Draft (lbs)	Energy Output (Cal/hr)		Energy Expense (Cal/hr)			Efficiency of Work (%)			Cardiorespiratory Activities				Ratios			Room Temp. (°C)
		$Q_{w.a}$ (Work accomplished)	H.P. (Horse-Power)	Q_o (Overall energy)	Q_n (Net energy)	Q_a (Absolute energy)	O.E. (Overall efficiency)	N.E. (Net efficiency)	A.E. (Absolute efficiency)	Pulse (rate per min)	Respiration (rate per min)	Tidal Air (liters)	Ventilation rate (liters per min)	H.P./M lbs. (M = wt. of horse)	Draft/M lbs.	Q_o/Q_s	
(D) Shetland Pony No. 3 ♂. Age 2 years. Weight 589 lbs. (267 kgs). Walking at 2.2 miles per hour (59.00 meter per minute).																	
Standing	0	—	—	260	—	—	—	—	—	41.6	14.7	4.03	59	—	—	1.00	13
Walking	0	—	—	560	300	—	—	—	—	47.3	28.4	3.91	111	—	—	2.15	13
Working	25	94	0.15	827	567	267	11.4	16.6	35.2	49.6	36.2	4.01	145	.000255	.042	3.18	14
Working	50	188	0.29	1120	860	560	16.8	21.9	33.6	54.1	41.7	4.33	181	.000492	.085	4.31	13
Working	75	282	0.44	1401	1141	841	20.1	24.7	33.5	60.9	46.1	4.86	224	.000747	.127	5.39	13
Working	100	376	0.59	1693	1433	1133	22.2	26.2	33.2	65.7	48.7	5.97	291	.001002	.170	6.51	13
(E) Percheron Colt No. 37 ♂. Age 10 months. Weight 1052 lbs. (477 kgs). Walking at 2.2 miles per hour (59 0 meters per minute).																	
Standing	0	—	—	550	—	—	—	—	—	51.6	19.7	5.83	115	—	—	1.00	15
Walking	0	—	—	1158	608	—	—	—	—	55.2	35.1	6.06	213	—	—	2.11	14
Working	25	94	0.15	1461	911	303	6.4	10.3	31.0	56.9	40.5	6.23	252	.000140	.024	2.66	15
Working	50	188	0.29	1683	1133	525	11.2	16.6	35.8	60.7	45.6	6.34	289	.000276	.048	3.06	15
Working	75	282	0.44	1927	1377	769	14.6	20.5	36.7	65.4	47.6	6.46	308	.000418	.071	3 50	16
Working	100	376	0.59	2221	1671	1063	16.9	22.5	35.4	62.0	47.1	6.72	316	.000561	.095	4.04	14

Table 24.1a. Statistical Constants for Pony No. 2.

Pony No. 2—Speed 1.15 mi/hr = 30.85 meters/min.

Expt.	Total Energy Expended (Q_o)					Pulse Rate					Tidal Air (liters)					Ventilation Rate (lit./min.)				
	N	M	σ	P.E$_m$	V (%)	N	M	σ	P.E$_m$	V (%)	N	M	σ	P.E$_m$	V (%)	N	M	σ	P.E$_m$	V (%)
Standing	7	241	30.2	±8	12.5	7	40.3	1.89	±0.5	4.7	7	5.50	0.374	±0.10	6.8	7	80.9	11.95	±3.3	14.8
Walking	7	527	33.0	±9	6.3	7	43.4	2.75	±0.8	6.3	7	5.67	0.534	±0.15	9.4	7	122.4	19.64	±5.4	16.1
25	5	659	35.7	±12	5.4	5	46.4	2.33	±0.8	5.0	5	6.00	0.537	±0.18	9.0	5	144.4	26.40	±8.9	18.[illegible]
50	5	820	38.1	±13	4.6	5	46.4	2.33	±0.8	5.0	5	6.06	0.467	±0.16	7.7	5	172.4	9.13	±3.1	5.[illegible]
75	5	927	45.2	±15	4.9	5	49.2	4.31	±1.5	8.8	5	5.90	0.126	±0.04	2.1	5	199.2	25.31	±8.5	12.7
100	5	1056	72.6	±24	6.9	5	51.2	5.31	±1.8	10.4	5	6.26	0.233	±0.08	3.7	5	225.6	28.28	±9.5	12.5
125	5	1283	54.3	±18	4.2	5	57.2	2.40	±0.8	4.2	5	6.96	0.174	±0.06	2.5	5	283.2	25.86	±8.7	9.1
150	5	1518	100.5	±34	6.6	5	60.0	4.38	±1.5	7.3	5	7.32	0.449	±0.15	6.1	5	283.2	34.83	±11.7	12.[illegible]
175	5	1575	64.6	±22	4.1	5	60.4	5.99	±2.0	9.9	5	7.44	0.344	±0.12	4.6	5	332.2	27.05	±9.1	8.1

N = Number of data points represented in average.

$M = \text{Mean} = \dfrac{\Sigma X}{N}.$

$\sigma = \text{Standard deviation} = \sqrt{\dfrac{\Sigma d^2}{N}} = \sqrt{\dfrac{\Sigma X^2}{N} - (Mx)^2}$

$\text{P.E}_m = \text{Probable error of mean} = \dfrac{.6745\sigma}{\sqrt{N-1}}.$

$\text{V}\ (\%) = \text{Percent variation} = \dfrac{\sigma}{M} \times 100.$

Table 24.2. Data for Percheron Gelding No. 19. Age 4½ years.

Expt.	Draft (lbs)	Energy Output (Cal/hr)		Energy Expense, (Cal/hr)			Efficiency of Work (%)			Cardiorespiratory Activities				Ratios			Room Temp (°C)
		Q_w = Work accomplished	H.P. (Horse-Power)	Q_o (Overall energy)	Q_n (Net energy)	Q_a (Absolute energy)	O.E. (Overall efficiency)	N.E. (Net efficiency)	A.E. (absolute efficiency)	Pulse (rate per min)	Respiration (rate per min)	Tidal Air (liters)	Ventilation rate (liters per min)	H.P./M lbs (M = wt. of horse)	Draft/M lbs	Q_o/Q_s	
(A) Walking at 1.15 miles per hour (30.85 meters per minute). Body weight 1514 lbs. (687 kgs).																	
Standing	0	—	—	548	—	—	—	—	—	36.8	10.6	9.68	103	—	—	1.00	16
Walking	0	—	—	1174	626	—	—	—	—	41.3	26.7	8.74	233	—	—	2.14	16
Working	50	98	0.15	1383	835	209	7.1	11.7	46.9	40.4	31.2	8.61	269	.000099	.033	2.52	14
Working	75	147	0.23	1558	1010	384	9.4	14.6	38.3	40.4	32.7	8.87	290	.000152	.050	2.84	16
Working	100	197	0.31	1698	1150	524	11.6	17.1	37.6	42.0	31.8	9.32	296	.000205	.066	3.10	16
Standing	0	—	—	637	—	—	—	—	—	45.8	17.3	7.94	137	—	—	1.00	28
Walking	0	—	—	1163	526	—	—	—	—	47.0	35.5	7.87	279	—	—	1.83	28
Working	125	246	0.38	1930	1293	767	12.7	19.0	32.1	51.1	35.4	10.13	359	.000251	.083	3.03	28
Working	150	295	0.46	1980	1343	817	14.9	22.0	36.1	52.9	35.1	10.11	355	.000304	.099	3.11	28
Working	175	344	0.54	2117	1480	954	16.2	23.2	36.1	51.2	35.4	10.80	382	.000357	.116	3.32	28
Working	200	393	0.61	2262	1625	1099	17.4	24.2	35.8	53.2	33.8	10.93	369	.000403	.132	3.55	29
Working	225	442	0.69	2362	1725	1199	18.7	25.6	36.9	53.3	36.1	10.89	393	.000456	.149	3.71	29
Working	250	492	0.77	2487	1850	1324	19.8	26.6	37.2	54.9	36.4	11.13	405	.000509	.165	3.90	28
Working	275	541	0.84	2752	2115	1589	19.7	25.6	34.0	55.3	36.8	11.92	439	.000555	.182	4.32	27
Working	300	590	0.92	2824	2187	1661	20.9	27.0	35.5	57.3	37.2	12.03	448	.000608	.198	4.43	27
Working	325	639	1.00	3095	2458	1932	20.6	26.0	33.1	58.4	37.4	12.18	455	.000661	.215	4.86	27
Working	350	688	1.07	3404	2767	2241	20.2	24.9	30.7	60.5	39.7	12.89	512	.000707	.231	5.34	28
Working	375	737	1.15	3577	2940	2414	20.6	25.1	30.5	61.4	39.7	13.16	523	.000760	.248	5.62	28
Working	400	787	1.23	3770	3133	2607	20.9	25.1	30.2	65.0	40.1	13.46	540	.000812	.264	5.92	27
Working	425	836	1.30	3999	3362	2836	20.9	24.9	29.5	66.0	41.4	13.74	569	.000859	.281	6.28	27
Working	450	885	1.38	3724	3176	2550	23.8	27.9	34.7	60.7	38.0	14.42	548	.000911	.297	6.80	20
Working	475	934	1.46	3939	3391	2765	23.7	27.5	33.8	60.0	38.5	14.20	547	.000964	.314	7.19	20
Working	500	983	1.53	4315	3767	3141	22.8	26.1	31.3	61.5	39.1	14.90	582	.001011	.330	7.87	20
(B) Walking at 2.2 miles per hour (59.00 meters per minute). Body weight 1530 lbs. (694 kg).																	
Standing	0	—	—	553	—	—	—	—	—	40.8	13.6	8.52	116	—	—	1.00	20
Walking	0	—	—	1422	869	—	—	—	—	43.6	31.9	9.34	298	—	—	2.57	22
Working	50	188	0.29	1850	1297	428	10.2	14.5	43.9	46.0	39.5	9.70	383	.000190	.033	3.35	22
Working	75	282	0.44	2042	1489	620	13.8	18.9	45.4	46.8	40.4	10.23	413	.000288	.049	3.69	22
Working	100	376	0.59	2368	1815	946	15.9	20.7	39.7	47.2	38.5	10.93	421	.000386	.065	4.28	22
Standing	0	—	—	670	—	—	—	—	—	43.2	16.8	7.98	134	—	—	1.00	28
Walking	0	—	—	1607	937	—	—	—	—	46.8	36.9	8.59	317	—	—	2.40	28
Working	125	470	0.73	2908	2238	1301	16.2	21.0	36.1	54.4	39.4	11.33	446	.000477	.082	4.34	28
Working	150	564	0.88	3113	2443	1506	18.1	23.1	37.5	56.6	39.6	12.25	485	.000575	.098	4.65	28
Working	175	658	1.03	3350	2680	1743	19.6	24.6	37.8	57.1	39.4	12.63	498	.000673	.114	5.00	28
Working	200	752	1.17	3651	2981	2044	20.6	25.2	36.8	61.6	39.7	12.61	500	.000765	.131	5.45	28
Working	225	846	1.32	4031	3361	2424	21.0	25.2	34.9	62.1	39.4	13.28	523	.000863	.147	6.02	27
Working	250	941	1.47	4232	3562	2625	22.2	26.4	35.8	64.4	41.7	14.23	593	.000961	.163	6.32	27
Working	275	1035	1.61	4650	3980	3043	22.3	26.0	34.0	66.9	41.9	14.34	601	.001052	.180	6.94	28
Working	300	1129	1.76	5008	4338	3401	22.5	26.0	33.2	66.6	41.8	14.42	602	.001150	.196	7.47	28
Working	325	1223	1.91	5400	4730	3793	22.6	25.9	32.2	63.3	47.7	14.16	675	.001248	.212	8.06	27
Working	350	1317	2.05	5651	4981	4044	23.3	26.4	32.6	69.2	47.3	14.90	704	.001340	.229	8.43	27
Working	375	1411	2.20	5752	5082	4145	24.5	27.8	34.0	69.5	47.4	15.35	727	.001438	.245	8.59	27
Working	400	1505	2.35	6337	5667	4730	23.7	26.6	31.8	73.0	50.4	16.22	818	.001536	.261	9.46	27
(C) Walking at 3.1 miles per hour (83.15 meters per minute). Body weight 1558 lbs. (707 kg).																	
Standing	0	—	—	531	—	—	—	—	—	42.7	11.5	8.98	103	—	—	1.00	17
Walking	0	—	—	1845	1314	—	—	—	—	44.8	39.2	10.64	417	—	—	3.47	18
Working	50	265	0.41	2256	1725	411	11.7	15.4	64.5	43.2	45.5	11.77	526	.000263	.032	4.25	17
Working	75	398	0.62	2623	2092	778	15.2	19.0	51.2	45.0	41.7	12.23	510	.000398	.048	4.94	16
Working	100	530	0.83	2915	2384	1070	18.2	22.2	49.5	47.0	41.0	12.80	516	.000533	.064	5.49	17
Standing	0	—	—	705	—	—	—	—	—	44.2	17.6	7.85	136	—	—	1.00	27
Walking	0	—	—	2130	1425	—	—	—	—	51.4	48.1	9.78	468	—	—	3.02	27
Working	125	663	1.03	3859	3154	1729	17.2	21.0	38.3	56.6	47.2	12.67	598	.000661	.080	5.47	27
Working	150	795	1.24	4320	3615	2190	18.4	22.0	36.3	58.7	46.2	13.23	613	.000796	.096	6.13	27
Working	175	928	1.45	4523	3818	2393	20.5	24.3	38.8	60.9	47.2	13.29	627	.000931	.112	6.42	27
Working	200	1061	1.65	4833	4128	2703	22.0	25.7	39.2	59.6	46.7	13.62	634	.001059	.128	6.86	28
Working	225	1193	1.86	5410	4705	3280	22.1	25.4	36.4	65.7	47.4	14.10	672	.001194	.144	7.67	28
Working	250	1325	2.07	5800	5095	3670	22.8	26.0	36.1	70.0	48.8	13.60	663	.001329	.160	8.23	28
Working	275	1458	2.27	6271	5566	4141	23.2	26.2	35.2	67.4	50.0	14.21	711	.001457	.176	8.90	28
Working	300	1590	2.48	6719	6014	4589	23.7	26.4	34.6	66.8	48.2	15.45	744	.001592	.193	9.53	28
Working	325	1723	2.69	7029	6324	4899	24.5	27.2	35.2	70.4	48.3	16.02	774	.001727	.209	9.97	27
Working	350	1855	2.89	7416	6711	5286	25.0	27.6	35.1	74.4	48.9	16.13	788	.001858	.225	10.52	27
Working	375	1988	3.10	7997	7292	5867	24.9	27.3	33.9	74.3	49.8	16.52	824	.001990	.241	11.34	28
Working	400	2120	3.31	8699	7994	6569	24.4	26.5	32.3	85.3	49.8	18.48	921	.002125	.257	12.34	23

Table 24.2a. Statistical Constants for Percheron Gelding No. 19.
Speed 1.15 miles per hour = 30.85 meters per minute.

Expt.	Total Energy Expended (Q_0)					Pulse Rate					Tidal Air (liters)					Ventilation Rate (lit./min.)				
	N	M	σ	P.E$_m$	V (%)	N	M	σ	P.E$_m$	V (%)	N	M	σ	P.E$_m$	V (%)	N	M	σ	P.E$_m$	V (%
Standing	5	548	48	±16	8.8	5	36.8	1.60	±0.5	4.4	5	9.7	1.13	±0.4	11.7	5	103	4.3	±2	4.
Walking	5	1174	98	±33	8.4	6	41.3	1.58	±0.5	3.8	5	8.7	0.59	±0.2	6.7	5	233	31.3	±11	13.
50 lbs.	10	1383	116	±26	8.4	10	40.4	1.20	±0.3	3.0	9	8.6	0.51	±0.1	6.0	9	269	27.7	±7	10.
75 lbs.	10	1558	137	±31	8.8	10	40.4	1.74	±0.4	4.3	10	8.9	0.66	±0.2	7.4	10	290	30.1	±7	10.
100 lbs.	10	1698	131	±30	7.7	10	42.0	1.55	±0.3	3.7	10	9.3	0.77	±0.2	8.3	10	296	28.7	±7	9.
Standing	34	637	92	±11	14.5	36	45.8	4.00	±0.5	8.7	34	7.9	0.61	±0.1	7.7	34	138	14.1	±2	10.
Walking	35	1163	88	±10	7.5	36	47.0	3.12	±0.4	6.6	34	7.9	0.52	±0.1	6.6	34	279	28.6	±3	10.
125 lbs.	9	1930	91	±22	4.7	9	51.1	4.14	±1.0	8.1	10	10.1	0.80	±0.2	7.9	10	359	47.0	±11	13.
150 lbs.	9	1980	101	±24	5.1	9	52.9	2.98	±0.7	5.6	10	10.1	0.88	±0.2	8.7	10	355	26.4	±6	7.
175 lbs.	9	2117	86	±20	4.0	9	51.2	3.43	±0.8	6.7	9	10.8	1.38	±0.3	12.8	9	382	39.8	±10	10.
200 lbs.	12	2262	72	±15	3.2	12	53.2	3.05	±0.6	5.7	12	10.9	0.78	±0.2	7.2	12	369	25.0	±5	6.
225 lbs.	13	2362	187	±36	7.9	13	53.3	4.07	±0.8	7.6	14	10.9	0.51	±0.1	4.7	14	393	37.2	±7	9.
250 lbs.	13	2487	137	±27	5.5	13	54.9	3.41	±0.7	6.2	13	11.1	0.68	±0.1	6.1	13	406	30.6	±6	7.
275 lbs.	8	2752	128	±33	4.7	8	55.3	2.97	±0.8	5.4	10	11.9	0.74	±0.2	6.2	10	439	35.8	±8	8.
300 lbs.	9	2824	107	±26	3.8	9	57.3	3.09	±0.7	5.4	10	12.0	0.79	±0.2	6.5	10	448	63.4	±14	14.

N = Number of data points represented in average.

$$M = \text{Mean} = \frac{\Sigma X}{N}.$$

$$\sigma = \text{Standard deviation} = \sqrt{\frac{\Sigma X^2}{N} - (M_x)^2}.$$

$$\text{P.E}_m = \text{Probable error of the mean} = \frac{.6745\sigma}{\sqrt{N-1}}.$$

$$\text{V (\%)} = \text{Percent variation} = \frac{\sigma}{M} \times 100.$$

Table 24.3a. Energy and Hypothetical Monetary Expenses for a Typical 1500-pound Work Horse and a Typical Ignition Type Farm Tractor.
It is assumed that the horse pulls 150 pound draft at 2.5 mph, or works at the rate of 1 horse-power. The tracto works at 12 H.P. with a gross efficiency of 13.4%

Hours work in 24	12	10	8	6	4	2	0
Hours rest in 24	12	14	16	18	20	22	24
I. Horse							
1. Work Accomplished							
H.P.-hours	12	10	8.0	6.0	4.0	2.0	0.0
K.W.-hours	8.9	7.5	6.0	4.5	3.0	1.5	0.0
Calories	7700	6420	5140	3850	2570	1280	0.0
2. Energy Expended							
Calories	46600	41300	35900	30600	25200	19900	14600
Lbs TDN	25.7	22.8	19.8	16.9	13.9	11.0	8.0
Factor correcting expended energy for activity during rest Qr = 1.25Qs	1.04	1.05	1.07	1.09	1.12	1.17	1.25
3. All day energetic efficiency (%)	16.5	15.5	14.3	12.6	10.2	6.4	0.0
4. Calories per H.P.-hour	3890	4130	4490	5100	6300	9940	∞
5. Calories per K.W.-hour	5210	5540	6010	6840	8450	13300	∝
6. TDN per H.P.-hour (lbs)	2.14	2.28	2.48	2.82	3.48	5.50	∞
7. TDN per K.W.-hour (lbs)	2.87	3.06	3.32	3.78	4.66	7.37	∞
8. Cost of TDN per H.P.-hour (at TDN $1.00 per 100 lbs)	2.14¢	2.28¢	2.48¢	2.82¢	3.48¢	5.50¢	

Table 24.3a.—*Continued.*

Hours work in 24	12	10	8	6	4	2	0
Hours rest in 24	12	14	16	18	20	22	24
II. Tractor							
1. Work Accomplished							
H.P.-hour	144	120	96	72	48	24	0.0
K.W.-hours	107	90	72	54	36	18	0.0
Calories	92600	77100	61600	46300	30800	15400	0.0
2. Energy Expended							
Calories	690000	575000	460000	345000	230000	115000	0.0
Gals fuel	20.0	16.7	13.4	10.0	6.7	3.3	0.0
3. All-day Efficiency	13.4	13.4	13.4	13.4	13.4	13.4	0.0
4. Calories per H.P.-hour	4800	4800	4800	4800	4800	4800	∞
5. Calories per K.W.-hour	6420	6420	6420	6420	6420	6420	∞
6. Fuel per H.P.-hour (gals)	.139	.139	.139	.139	.139	.139	∞
7. Fuel per K.W.-hour (gals)	.186	.186	.186	.186	.186	.186	∞
8. Cost of fuel plus oil per H.P.-hour (fuel at 10¢ per gal, 20% for oil)	1.7¢	1.7¢	1.7¢	1.7¢	1.7¢	1.7¢	
III. Horse vs tractor							
1. Ratio: TDN cost per H.P.-hour for horse to fuel and oil cost per H.P.-hr for tractor	1.26	1.34	1.46	1.66	2.05	3.24	
2. Cost per 100 lbs. TDN for above ratio to equal one (horse feed cost = tractor fuel cost)	79¢	74¢	68¢	58¢	49¢	31¢	

Table 24.3b. Estimated Yearly Costs other than Fuel for Horse and Tractor.

	per horse	Per 12 H.P. ignition type tractor
Depreciation	$7.00	$101.00
Interest and taxes	5.00	7.00
Chore Labor	5.00	7.00
Harness or Repair	3.00	2.00
Housing	2.00	3.00
Total	$22.00	$120.00
Cost per day	0.063	0.329
Cost per H.P.	0.063	0.027

Table 24.3c. Distribution of Expenses for Maintaining a Work Horse in Missouri.

Item	Cost	Per cent
All feed	$44.42	66.0
Depreciation	6.96	10.3
Interest, Insurance and Taxes	5.56	8.3
Chore Labor (working only)	4.73	7.0
Harness	3.33	5.0
Housing	2.31	3.4
Total	$67.31	100

Table 24.3d. The Influence of the Number of Hours Worked on the Cost of Work per Hour.

Hours worked per year	No. of farms in group	Feed cost per horse per year	Total cost per horse per year	Cost per hour of horse labor
200– 350	3	$41.02	$59.03	$0.203
351– 500	11	46.74	67.25	0.145
501 - 650	13	45.04	63.76	0.114
651– 800	15	41.63	64.00	0.090
801– 950	11	43.23	69.75	0.079
951–1100	6	48.40	74.75	0.073
1101–1250	4	44.27	73.20	0.064
1401–1700	3	49.77	86.23	0.054

Table 24.3e. Pounds Digestible Nutrients Required by Horses of Different Live Weights Working Different Number Hours per Day.*

(Supplement to Fig. 24.19)

Hours worked per day	Body Weight											
	600	700	800	900	1000	1100	1200	1300	1400	1500	1600	1700
0	5.7	6.3	7.0	7.6	8.2	8.8	9.4	9.9	10.5	11.0	11.6	12.1
1	6.1	6.8	7.6	8.3	8.9	9.6	10.3	10.9	11.5	12.1	12.8	13.4
2	6.6	7.3	8.2	8.9	9.7	10.4	11.2	11.8	12.6	13.2	14.0	14.6
3	7.0	7.8	8.8	9.6	10.4	11.3	12.1	12.8	13.6	14.3	15.2	15.9
4	7.5	8.4	9.4	10.3	11.2	12.1	13.0	13.8	14.7	15.5	16.4	17.1
5	7.9	8.9	10.0	10.9	11.9	12.9	13.8	14.7	15.7	16.6	17.5	18.4
6	8.4	9.4	10.6	11.6	12.7	13.7	14.7	15.7	16.7	17.7	18.7	19.7
7	8.8	9.9	11.2	12.3	13.4	14.5	15.6	16.6	17.8	18.8	19.9	20.9
8	9.3	10.5	11.8	13.0	14.1	15.3	16.5	17.6	18.8	19.9	21.1	22.2
9	9.7	11.0	12.3	13.6	14.9	16.2	17.4	18.6	19.9	21.0	22.3	23.5
10	10.2	11.5	12.9	14.3	15.6	17.0	18.3	19.6	20.9	22.1	23.5	24.7
11	10.6	12.0	13.5	15.0	16.4	17.8	19.2	20.5	21.9	23.3	24.7	26.0
12	11.1	12.5	14.1	15.6	17.1	18.6	20.1	21.5	23.0	24.4	25.9	27.3

* Computed from the equation TDN = $0.053\ M^{0.73} + 1.27$ (H.P.-hr.) assuming that tractive pull of loa
10% of body weight and the speed was 2.2 miles per hour.

Table 24.3f. Pounds Digestible Nutrients Required by Horses of Different Live Weights Doing Different Amount of Work.*

(Supplement to Fig. 24.19)

H.P. hrs. work/day	Body Weight													
	600	700	800	900	1000	1100	1200	1300	1400	1500	1600	1700	1800	1900
0	5.7	6.3	7.0	7.6	8.2	8.8	9.4	9.9	10.5	11.0	11.6	12.1	12.6	13.1
1	6.9	7.6	8.2	8.9	9.5	10.1	10.6	11.2	11.8	12.3	12.8	13.4	13.9	14.4
2	8.2	8.9	9.5	10.1	10.8	11.3	11.9	12.5	13.0	13.6	14.1	14.6	15.2	15.7
3	9.5	10.1	10.8	11.4	12.0	12.6	13.2	13.8	14.3	14.8	15.4	15.9	16.4	16.9
4	10.7	11.4	12.0	12.7	13.3	13.9	14.5	15.0	15.6	16.1	16.6	17.2	17.7	18.2
5	12.0	12.7	13.3	14.0	14.6	15.2	15.7	16.3	16.8	17.4	17.9	18.4	19.0	19.5
6	13.3	14.0	14.6	15.2	15.8	16.4	17.0	17.6	18.1	18.6	19.2	19.7	20.2	20.7
7		15.2	15.9	16.5	17.1	17.7	18.3	18.8	19.4	19.9	20.5	21.0	21.5	22.0
8			17.1	17.8	18.4	19.0	19.5	20.1	20.6	21.2	21.7	22.2	22.8	23.3
9				19.0	19.6	20.2	20.8	21.4	21.9	22.5	23.0	23.5	24.0	24.6
10					20.9	21.5	22.1	22.6	23.2	23.7	24.3	24.8	25.3	25.8
11							23.4	23.9	24.5	25.0	25.5	26.1	26.6	27.1
12									25.7	26.3	26.8	27.3	27.9	28.4
13										27.5	28.1	28.6	29.1	29.6
14												29.9	30.4	30.9
15													31.7	32.2
16														33.4
17														

* Computed from the equation TDN = $0.053\ M^{0.73} + 1.27$ (H.P.-Hr.) in which TDN is pounds di
nutrients, M body weight in pounds, H.P.-Hr. is horse-power-hours of work.

le 24.4. Relative Rise of Oxygen Consumption (Metabolism) and Cardiorespiratory Activities with Increasing Rate of Work (Horse Power) and Load

he standing values are taken as the base values, represented as 100%, and the other values as percentages of e base values. The original data and statistical constants are listed in Table 24.2.

Work rate (horse power)	Pulling draft (lbs.)	O_2 consumption (metabolic rate) (%)	Pulse Rate (%)	Respiration rate (%)	Tidal air (%)	Ventilation rate (%)
Percheron Gelding #19 walking at 1.15 miles per hour.						
Standing	0	100	100	100	100	100
Walking No load	0	214	112	232	[illegible]	[illegible]
[illegible]	50	[illegible]	110	294	[illegible]	[illegible]
[illegible]	75	[illegible]	110	308	92	[illegible]
[illegible]	100	[illegible]	114	300	[illegible]	[illegible]
Standing	0	114	[illegible]	163	[illegible]	[illegible]
Walking No load	0	212	[illegible]	335	[illegible]	[illegible]
[illegible]	125	[illegible]	[illegible]	334	[illegible]	[illegible]
[illegible]	150	[illegible]	144	331	104	[illegible]
[illegible]	175	[illegible]	[illegible]	334	112	[illegible]
[illegible]	200	[illegible]	[illegible]	319	[illegible]	[illegible]
[illegible]	225	[illegible]	[illegible]	340	112	[illegible]
[illegible]	250	454	[illegible]	343	115	[illegible]
[illegible]	275	502	[illegible]	347	122	[illegible]
[illegible]	300	[illegible]	[illegible]	351	124	[illegible]
[illegible]	325	[illegible]	[illegible]	353	[illegible]	[illegible]
[illegible]	350	[illegible]	[illegible]	374	[illegible]	[illegible]
[illegible]	375	[illegible]	[illegible]	374	[illegible]	[illegible]
[illegible]	400	[illegible]	[illegible]	379	[illegible]	[illegible]
[illegible]	425	[illegible]	[illegible]	360	142	[illegible]
[illegible]	450	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	475	[illegible]	[illegible]	[illegible]	147	[illegible]
[illegible]	500	[illegible]	[illegible]	[illegible]	154	[illegible]
Percheron Gelding #19 walking at 2.2 miles per hour.						
—	0	100	100	100	100	100
—	0	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	50	[illegible]	[illegible]	[illegible]	114	[illegible]
[illegible]	75	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	100	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
—	0	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
—	0	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	125	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	150	[illegible]	[illegible]	[illegible]	144	[illegible]
[illegible]	175	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	200	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	225	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	250	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	275	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	300	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	325	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	350	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	375	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	400	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Percheron Gelding #19 walking 3.1 miles per hour.						
—	0	100	100	100	100	100
—	0	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
—	0	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
—	0	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	174	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	174	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Table 24.4. *Continued.*

Work rate (horse rate)	Tractive draft (lbs)	O_2 consumption (metabolic rate) (%)	Pulse rate) (%)	Respiration rate (%)	Tidal air (%)	Ventilation rate (%)
Shetland Pony #2 walking 1.15 miles per hour.						
—	0	100	100	100	100	100
—	0	219	108	146	103	151
0.08	25	273	115	163	109	178
0.15	50	340	115	193	110	212
0.23	75	385	122	229	107	246
0.31	100	438	127	246	114	279
0.38	125	532	142	277	127	349
0.46	150	630	149	263	133	349
0.54	175	654	150	303	135	410
Shetland Pony #2 walking 2.2 miles per hour.						
—	0	100	100	100	100	100
—	0	244	110	166	108	182
0.15	25	321	117	218	108	238
0.29	50	411	127	266	114	308
0.44	75	522	137	319	115	369
0.59	100	638	156	335	126	428
0.73	125	802	154	333	146	491
0.88	150	970	177	369	150	560
Shetland Pony #3 walking 1.15 miles per hour.						
—	0	100	100	100	100	100
—	0	182	101	137	95	131
0.08	25	246	108	182	94	170
0.15	50	299	115	186	100	185
0.23	75	342	113	215	98	209
0.31	100	416	134	236	108	255
0.38	125	471	136	254	111	280
0.46	150	583	151	238	128	306
Shetland Pony #3 walking 2.2 miles per hour.						
—	0	100	100	100	100	100
—	0	215	114	193	97	188
0.15	25	318	119	246	100	246
0.29	50	431	130	284	107	307
0.44	75	539	146	314	114	380
0.59	100	651	158	331	121	493
Percheron Colt #37 walking 2.2 miles per hour.						
—	0	100	100	100	100	100
—	0	211	107	178	104	185
0.15	25	266	110	206	107	219
0.29	50	306	117	231	109	251
0.44	75	350	127	242	111	268
0.59	100	404	120	239	115	275

Chapter 25

Summary and Integrating Discussion

25.1: Summary

> Human beings possess a capacity which is entirely peculiar to them—the capacity to summarize the experience of the past. *Alfred Korzybski*

As indicated by the title of this book, our original material is on energy and nitrogen metabolism (Chs. 13–15) including some bioenergetic methods (Ch. 12), on energetic efficiency of productive processes (Chs. 3, and 21–24), and on various aspects of growth (Ch. 16), aging (Ch. 18) which we consider as inseparable from growth, on the interrelation between part and whole (Ch. 17) which we consider inseparable from the relation of energy metabolism to size (Chs. 13 to 15), and on physiological time and equivalence of age (Ch. 19).

Naturally, the factors influencing efficiency were analyzed, such as the influence of plane of nutrition (Chs. 4 and 5), metabolic catalysts, including enzymes, minerals, and vitamins (Ch. 6), hormones (Ch. 7), season (Ch. 8), time of day (Ch. 9), temperature (Ch. 11), and nutritional balance (Ch. 20). Likewise, the factors influencing profit were discussed with special reference to plane of nutrition (Ch. 5), body size (Ch. 22), productive plane ("dairy merit" in cattle, Ch. 22, muscular work in horses, Ch. 24, egg production, Ch. 23).

Many of the problems discussed have not yet been investigated. Such is the influence of the immediate efficiency and profit on longevity and fertility (long-range efficiency and profit). Is unusually rapid growth associated with early aging? Is hard muscular work associated with early aging? Is unusually high milk or egg production associated with early mortality or disability? These questions are difficult to answer categorically because in most cases the exceptionally high productive level under "average" conditions is the result of a sound body which normally favors longevity and fertility. If, however, the productive level of a given animal is accelerated by special methods, longevity and fertility may well be reduced. Thus accelerating winter egg production by artificial illumination increases the mortality rate; dairy cows may be "burned out" prematurely by forced high milk production; the hard working farm or mine horse does not live as long as the country gentleman's carriage horse.

The theoretical feature of this book is the attempt to generalize large bodies of cumbersome data by simple rational but broadly inclusive equations. Thus the relative-growth equation, $Y = aX^b$, relating part, Y, to whole X (Ch. 17), or of energy and endogenous nitrogen catabolism, Y, to body weight X (Chs. 13 and 14), or maintenance cost Y to body weight X (Ch. 15), or milk or egg production, Y, to body weight X (Chs. 21–23), are based in one case (Ch. 17) on animals ranging from mice to whales, and in another (Ch. 13), from mice to elephants, thus giving the results general validity.

Similarly, the growth and aging equations $Y = Ae^{kt}$, $Y = Ae^{-kt}$, and $Y = A - Be^{-kt}$, relating body size, or population size, or aging, Y, to age or time t (Chs. 16–19) are applicable to species ranging from mice to large farm animals and to populations from bacteria to humans. Equivalence charts indicate species similarities and differences (Ch. 19) and point out the significance of the concept of physiologic time as contrasted to physical time (Ch. 19).

The above growth equation for the self-inhibiting phase (Sect. 16.5) also represents the principle of diminishing increments (Ch. 5), relating net energy produced (milk production, meat production, egg production, muscular work) to gross energy (feed) consumed (Figs. 1.1 to 1.3).

The theoretical analyses brought many bits of agriculturally useful information as, for example, how metabolism and maintenance costs vary with age and weight (Chs. 13–15); how pulmonary ventilation and water vaporization vary with weight and age (Ch. 14); how to measure the cardiorespiratory reserve for muscular work in animals ranging from mice to elephants (Ch. 24); how temperature influences productive processes (Ch. 11); how to evaluate the partition of feed consumed between maintenance, growth, milk production (Ch. 21) and egg production (Ch. 23); how the plane of nutrition influences the efficiency and profit on milk production (Chs. 5 and 22); how body size of cattle influences energetic efficiency and profit on milk production; the relative energetic efficiency of milk, egg, and meat production (Ch. 3). To elaborate on the last point, milk production is the most efficient of the three processes. Up to 50 per cent of the consumed *TDN* (total digestible nutrients) energy may be converted into milk (Chs. 3, 21, 22), twice as high as for the maximum possible efficiency of egg production (Ch. 23) and several times as high as for beef production (the efficiency of meat production is high, about 30%, shortly after birth but it declines rapidly thereafter with increasing age (Ch. 3). These are not arguments in favor of milk or against eggs or beef production, because the consumption of egg and beef is not on the basis of economy alone. If economic feeding were the only consideration, the method of India and China—feeding on whole cereals and vegetables—would be preferred; the second most economic method is that practiced in much of eastern Europe and in parts of Africa where whole cereals and milk (and cheese) are the staples.

Energetic efficiency of conversion is not the only consideration in the choice of animals and animal products. Beef production may be from the technical energetic viewpoint wasteful, but practically economical because the beef may be produced largely on grazing, utilization of forage which would otherwise be wasted. The same is true of many other processes. Thus a horse may be less efficient energetically than a Diesel engine but the farmer does not have to pay for the horse fuel or for the horse; the forage grows on the farm and the horse reproduces and repairs himself.

The productive level is a very important aspect of the profitableness of an enterprise. While the maximum efficiency of milk production is 50 per cent, most "good" cows produce milk at an efficiency of only 25 per cent which just about pays for the dairyman's labor, feed, and other expenses. "Making money" in the dairy business involves greater efficiency of milk production. A 33 per cent efficiency indicates a "superior" dairy cow, and a profitable one (Ch. 22). But the profit is complicated by body size and related factors.

The size of the dairy cow is not a factor in the *energetic-efficiency* complex—rats, goats, small and large dairy cows and even women, tend to produce milk at the same *energetic* efficiency; but size (and related considerations) is an important factor in the *monetary-profit* complex. If the energetic efficiencies and other conditions are equal, the larger the animal the greater the milk return per unit human labor expended because it does not take much more time or labor to milk, feed, clean, rear, and manage a large than a small animal. Thus to produce 1000 lb of milk (of 4% fat) at 30 per cent energetic efficiency, it requires (Ch. 22) 26 of 1700-lb cows, or 30 of 1400-lb cows, or 38 of 1000-lb cows, or 42 of 900-lb cows, or 53 of 700-lb cows, or 200 of 100-lb goats; and it obviously takes more labor to milk, feed, etc., 200 goats than 53 cows, 53 cows than 38 cows, 38 than 26 cows, and so on.

25.2: Integrating discussion.

> If we could first know where we are and whither we are tending, we could better judge what to do and how to do it. *Abe Lincoln*
>
> The tower of Babel was a part of a plan to penetrate Heaven . . . magnificent . . . but it ended in confusion. *Willard H. Dow*

The progress in agricultural production is inseparable from the progress of science, and industry; and the 150-fold increase of the human population in the past 300 years in what we now call U. S. A. is a direct consequence of the progress in agricultural production. All our present social, economic, political, military and related problems are tied up with the growth of our population dependent on the progress of science, agriculture and industry. It may be useful to discuss some of these interrelations in summary fashion from the viewpoints of homeostatis and organismic theory (Ch. 10), growth (Ch. 16), and thermodynamics (Ch. 2).

It was shown in Chapter 10 on homeostasis that while the animal body is made up of a very unstable stuff (protoplasm), and while the sheer process of living produces incessantly substances—such as carbonic acid, sulfuric acid, phosphoric acid, and related wastes—highly destructive to protoplasm, yet the body maintains a remarkably uniform "internal environment" and a stable pattern, in the case of man for perhaps a hundred years. The living body is evidently equipped with extremely efficient devices for maintaining constant its "physiological constants" despite many vicissitudes.

The concept of physiologic homeostasis in the individual organism was extended in Section 10.9 to include social homeostasis. This section is an extension of Section 10.9 on social homeostasis to agricultural developments and to the past, present, and future growth of the human population in the U. S. A.

The growth curve of the human population in the U. S. A. was discussed in detail in Section 16.8, and illustrated graphically in Figs. 16.56A to C. We now proceed from where we left off in Sections 10.9 and 16.8. In this connection Fig. 18.1a on the time changes in age distribution of the human population is also significant.

The human population in what is now called the U. S. A. numbered about 1 million at the time of Columbus' arrival (450 years ago) or the Pilgrims' arrival (300 years ago). From the principle of population growth (Sect. 16.5: the biotic power of an animal is limited only by the repressive forces in the environment) the population then numbered 1 million only because the environment would not permit a larger population. Our present population is about 133 million, and curve 1 in Fig. 16.56b shows that it will be about 160 million within 50 years, by the year 2000. Thompson's recent book,[17] substantiates this prediction.

The rise of this population was evidently associated with the coming of Europeans. How did the coming of Europeans expand the population-supporting capacity 150-fold?

First, Europeans introduced new prime movers, the horse and ox. These freed man from much heavy physical labor, thereby enabling him to cultivate more land per man. Second, the Europeans stabilized food production by systematic cultivation, introducing improved domesticated plants and animals which need less land and time per unit food production than wild animals hunted by the Indian. It saves time to have the animals and plants in one place rather than to have to hunt for them.

The North American Indian had apparently only one domestic animal, the dog. The Indian also hunted the wild turkey, partridge, pigeon, goose, duck, deer, buffalo. The North American Indian had wild crabapples, cherries, grapes, strawberries, cranberries, gooseberries, huckleberries, raspberries, blackberries; he had cultivated maize (corn), beans, peanuts, potatoes ("Irish" and sweet), pumpkin, and some varieties of cotton. Europeans introduced horses, cattle, sheep, goats, domestic fowls; wheat, rye, barley, oats, peas, and most of the fruits; and improved the Indians' cultivated crops.[1]

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[1] South America had other animals and also plants such as tomatoes and peppers, and South America had a population of, perhaps, 8 million as contrasted to 1 million in North America.

The stupendous increase in the North American population is due, however, not so much to the introduction of European animals, plants, and knowledge as such, as to the European method and tradition of incessantly *creating new knowledge*—the invention of invention—and immediately applying it to the business of producing the things which ordinarily limit population growth—food, shelter, transportation, and communication. The period of rapid population expansion in North America is associated with what is called the Industrial Revolution (1770–1840) and with the wonderful nineteenth century of ever more rapid growth of machine technology and factory methods.

Beginning with the introduction of Arkwright and Cartwright's mechanical spinning and weaving methods, which revolutionized the textile industry between 1770 and 1780, there followed Eli Whitney's cotton gin (1793) for separating seed from cotton which made the United States a great exporting country and revived slavery; Fulton's steamboat (1807) lead to the development of the canals and the river cities, New Orleans, St. Louis, Cincinnati, Pittsburg; then the railroad:[2] in 1830 there was built the 11-mile Baltimore & Ohio along which chugged trains at a speed of 13 miles per hour. These 11 miles of 1830 grew to 30,000 miles by 1860. In the same period, 1830–1860, came John Deer's steel plow, McCormick's reaper and thresher, the grain drill, the grain elevator, mowing machine, the sewing machine, 2-horse straddle cultivator, the kerosene lamp (which crowded out the candle-making industry!).

In the next 30 years, 1870–1900, came the gang plow, silo, cream separator, combine harvester, the Babcock butter-fat tester (1890) which gave a new yardstick for evaluating dairy cattle. By 1900 came the automobile, tractor, airplane, electric power and electric communications. The horse is being replaced to a large extent by mechanical power at the expense of the "free" energy (Ch. 2) of petroleum stored in the past ages.

The perfection of the combine harvester is eliminating enormous numbers of farm hands; the mechanical cotton picker, not yet perfected but which undoubtedly soon will be, will eliminate hundreds of thousands of field hands, sharecroppers and small land owners; likewise as regards mechanical corn harvesters which pick and shell corn in one operation, forage harvesters, including side-delivery rakes and pick-up hay bales, and so on.

Such discoveries as chemical fertilizers, immune sera, antitoxins, insecticides, methods of control of infectious diseases, improvements of plants and animals by scientific breeding and artificial fertilization also eliminate human labor by increasing production, by making two blades of grass grow where one grew before. Thus hybrid corn increases the corn yield 20 per cent. It is said that a new hybrid corn is growing in a Mississippi locality at the rate of 130 bushels an acre, whereas, because of unfavorable temperature, ordinary corn produced only 20 bushels an acre.

The sum total is that ever more is produced by fewer farmers. In 1830, 50 to 60 man-hours were required to produce 20 bushels wheat from an acre; in 1925, 3 to 4 man-hours were required to produce 20 bushels of wheat from an acre.

Mechanization of urban industries has grown even more rapidly than that of agricultural production.

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[2] The steam engine was invented by James Watt (Glasgow) in 1785. The first English locomotive was made in 1804 and the first English railway was run in 1825. The first steamboat was run in England in 1802. The first steamship crossed the Atlantic in 1819.

These developments indicate the unique power of knowledge, especially the European tradition of accumulation of new knowledge and its application, and especially what Charles Kettering calls the capacity or experience of change-making. Science and technology is a continuously changing process. This new knowledge enabled the human population to increase some hundred-and-fifty fold above the original Indian population.

However, the percentage increase in population in the United States has been subsiding since 1880 (Fig. 16.56a and c). Thus the population gain during 1920–1930 was 17 million, whereas the gain between 1930–1940 was only 8 million, and it is rapidly approaching a ceiling (Fig. 16.56b). Why is the growth rate of our population declining? It is not due to the lack of food or other consumers' goods. Indeed, the apparent market surpluses (prior to the present war) are embarrassing in their magnitudes. Nor is it due to lack of "living space" because the population density in the U. S. A. is only about 40 persons per square mile (as contrasted, for example, to 670 in England and Wales, 665 in Belgium, 562 in Netherland, 347 in Germany, 340 in Italy, 320 in Japan, and so on).

Life in the U. S. A. is theoretically and could be actually extremely pleasant. Medical progress is freeing us from epidemic diseases, communication progress is giving us unlimited opportunity for social contacts, mechanical progress is freeing us from heavy labor, agricultural and nutritional progress is freeing us from malnutrition. Why, then, is the percentage increase in population declining?

The principle of homeostasis (Ch. 10) appears to substantiate the old suggestion that perhaps "everything seems pregnant with its contrary." Thus the development of ever better farm machinery, of course good in itself, displaces many farm workers. It is estimated that since 1787 the productivity per farmer (or mechanized farms) increased 60-fold (after deducting the time required to make the farm machinery); during the year 1935, about 345,000 farm workers were displaced on American farms by farm machinery and perhaps as result a million-odd farm families were receiving (1938) relief assistance. The relative decline in rural population, indicated by the following data, may be attributed to agricultural progress, to our ability to produce more food with fewer farm producers.

The decline in the number of agricultural producers is greater than is indicated by the following table. Of this rural population, perhaps only 20 per cent (rather than the indicated 43 per cent) is now employed in productive agriculture as contrasted to about 95 per cent in 1790. "Fifty per cent of all American farms produce only 10 per cent of our commercial farm products. More than a million and a half men and boys of working age who lived on farms in 1937 registered as partly or wholly unemployed" (H. R. Tolley).

This movement from the farm to city lead to repression in population growth because wife and children were economic assets on the farm but are liabilities in the city. When, in addition, living and especially educational standards

Relative Growth of Rural Populations[3] in the U. S. A.

Year	Total population (millions)	Rural population (millions)	Percentage rural population
1790	3.9	3.7	95
1800	5.3	5.0	94
1810	7.2	6.7	93
1820	9.6	8.9	93
1830	12.9	11.7	91
1840	17.1	15.2	89
1850	23.2	19.6	85
1860	31.4	25.2	80
1870	38.6	28.7	74
1880	50	36	72
1890	63	41	65
1900	76	46	60
1910	92	50	54
1920	106	52	49
1930	123	54	44
1940	132	57	43

are high, children become serious economic burdens with resultant delay in parenthood and therefore in birth-rate (Sect. 16.8). This movement from farm to city may, then, be the basic cause of declining birth rate, although subsidiary causes, such as changing attitudes to birth control may be important contributing factors.

Urban populations likewise tend to suffer from technological unemployment. Thus[4] while the electric-lamp production index *increased* from 100 in 1920 to 139 in 1930, the hours required to make the lamps *decreased* from 100 in 1920 to 32 in 1930.

War may be the blind social homeostatic mechanism for relieving unemployment in a society which cannot invent better methods for maintaining constant its "internal environment." The biology of war and the involved compensating homeostatic mechanisms have been discussed in Section 10.9 where it was pointed out that, among other factors, the greatest immediate need is development of methods for selecting leaders who will utilize the tools of science, which grow ever more powerful, for peaceful construction rather than for warlike destruction. This is by no means a new idea.[5]

In closing it may be useful to discuss the significance of the accelerated

[3] Department of Commerce, Bureau of the Census, Series P-3, 1941, and other publications.

[4] Baldwin, P. M., "Technological unemployment." *Scientific Monthly*, **40**, 44 (1935).

[5] See Plato's Republic. See also, for example, W. C. Mitchell (Harvard Tercentenary Publications, 1937), who advocates social control and invention by a national planning board; F. B. Jewett and R. W. King (University of Pennsylvania Press, Bicentennial Conference on "Engineering Progress and the Social Order," 1941), who advocates government guided by expert advisory agencies analogous to the research laboratories of modern business, and the many "blue prints" by Stuart Chase. See also: Lynd, R. S., "Knowledge for what?" Princetown University Press, 1939; Becker, Carl, "Progress and power," Stanford University Press, 1936. Stamp, Sir Josiah, "The science of social adjustment," London, 1937. Bernal, J. D., "The social function of science," New York, 1939.

agricultural and industrial production in the light of the laws of thermodynamics (Ch. 2), to view the bioenergetic situation as a whole.

According to the second law of thermodynamics, our prodigious increase in population and mechanization must be paid for by increase in free energy expenditure.

Our two energy sources are: A) non-renewable, gas, gasoline and other petroleum products, and coal; B) renewable, products of the farm, forest and stream, and hydroelectric energy. Let us discuss each briefly.

A. *Non-renewable energy sources.*—With relatively few exceptions, our machines—including our 30 million peace-time automobiles—are powered, directly or indirectly, by petroleum and coal energy. Such processes as iron manufacture and, of course, transportation, involve the consumption of enormous amounts of gas, oil, and coal. These energy forms are vegetable remains of the geologic past, fossil fuels not renewable under present conditions. While, therefore, the rise in the curve of energy consumption is usually considered as the best index of enrichment it is thermodynamically the best index of free-energy impoverishment.

At the present rate of consumption, the *known liquid* fuel reserves are estimated to last 20 years. There is also oil remaining to be discovered. The discovery of sufficient liquid fuel to last another 50 or 100 years or even several hundred years does not change the overall picture that we are approaching the end of the "free-energy" oil era. We are in a much better position with regards to low-grade coal reserves. The following statement of our energy resources is given by the National Resources Committee.[6]

> Our coal resources have been estimated (1937) at approximately 3000 billion tons, of which about half a billion tons is consumed annually. Our proven oil reserves have been estimated at 15 billion barrels of which about $1\frac{1}{4}$ billion barrels are consumed per year (during 1937). Our natural gas resources have been estimated at 60 to 100 trillion cubic feet (energy equivalent of about 17 billion barrels of petroleum), of which 2 trillion cubic feet are consumed per year (1937).
>
> It is estimated that energy consumption per capita in the United States is 50 per cent higher than in Great Britain, over 200 per cent higher than in Germany, over 1000 per cent over that in Japan, and over 1500 per cent over than in China. From 1889 to 1929 each year's energy consumption increased 60 per cent above that in the preceding year. Of this energy (in 1937), 48 per cent was derived from bituminous coal, 6 per cent anthracite coal, 32 per cent petroleum, 10 per cent natural gas, less than 4 per cent water power. The United States has produced about 60 per cent of all the petroleum consumed in the world, as indicated in the following table.

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[6] Energy resources and national policy. National Resources Committee, U. S. Government Printing Office, Washington, D. C., 1939. The ordinary peace-time annual per capita petroleum consumption is 450 gallon in the United States, 80 gallon in the United Kingdom, 50 gallon in the U. S. S. R. The rate of per capita petroleum consumption in the United States is 30 times that of the rest of the world. The petroleum consumption in the United States provides the work equivalent to 140 servants per family.

Oil Production,[7] 1940

	Million barrels per year	Percentage of world's production
United States	1406	63
Venezuela	223	10
Mexico	42	2
Rest of South America	82	3.6
Russia	242	11
Iran (Persia)	78	3.5
Dutch Indies	62	3.0
Roumania	41	1.8
Iraq (Syria)	13	0.6
Canada	10	0.4
Total North America	1457	65
Central and South America	305	13
Europe	296	13
Asia	113	5
Oceania	72	3
Total World production	2251	100

Outside of the renewable vegetation energy, the most important is hydroelectric energy. The outstanding United States hydroelectric projects are the Grand Coulee and Bonneville Dams on the Columbia River, the Boulder Dam in Colorado, the Norris, Hiawassee, and Hales Bar Dams on the Tennessee River and its tributaries, the Keokuk Dam across the Mississippi River, the Fort Peck Dam on the Missouri River in Montana, the Shasta Dam on the Sacramento River in Northern California, and the Niagara-Hudson hydroelectric power plants.

A hydroelectric project now under consideration is the St. Lawrence-Niagara Development, in connection with the Great Lakes–St. Lawrence Seaway project. It is proposed to harness the flow of the St. Lawrence River at Massena, New York, and Cornwall, Ontario, to yield $2\frac{1}{4}$ million horse power and to improve the existing Niagara Falls facilities to yield another $\frac{3}{4}$ million horse power. This power output is expected to give "a new lease on life to New York State industries, a source of cheap electricity which should make possible the resumption of manufacturing growth."[8] This power is said to be needed especially by electro-process industries, such as manufacture aluminum, ferro-alloys, carbides, dyes and other chemicals. Moreover, $\frac{3}{4}$ million horse power could be carried as far as New York City. The cost of the project ($1\frac{2}{3}$ billion dollars) would quickly pay for itself.

An attempt was made to utilize the water power from tides, especially in Maine (the Passamaquoddy Project), and one or two tide power plants are said to be in operation in Europe. This is a promising future source of renewable power.

Windmills are used, but the energy generated is relatively insignificant.

It has been suggested that temperature differences in the oceans, direct solar heat, and interatomic energy may be eventually utilized as sources of power. However, no substantial progress has thus far been made on these methods, and there are no encouraging signs that such will be made in the near future.[9]

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[7] Egloff, G., *Chem. & Eng. News*, **20**, 649 (1942).

[8] St. Lawrence Survey, U. S. Dept. Commerce.

B. *Renewable energy sources.*—It is said that we shall use alcohol and vegetable oils after the petroleum energy has been exhausted. This reminds one of Marie Antoinette's advice to the Paris poor to eat cake when they had no bread. Alcohol[10] and vegetable oils are, of course, more expensive than petroleum fuels. Moreover, if all our crops were converted to alcohol and oil, they would not supply the present rate of petroleum-energy consumption.[10a]

Furthermore, it appears that in spite of, or rather because of, the accelerated rate of agricultural production per man-hour of work, the agricultural productivity *per acre* is declining. Today, a man operating a tractor drawing a battery of plows can plow a hundred times the acreage he could a century ago with a walking plow; and there is a corresponding accelerated rate of soil erosion and removal of plant nutrients. The natural rate of soil formation is not equal to the rapid rate of soil and plant-nutrient removal by these mechanized methods. The mechanically-plowed ground loses as much of its soil in ten years as pasture in a 100 years.

There is, of course, disagreement among specialists concerning the cause and fate of declining soil fertility. To Whitney,[11] "the future seems most hopeful, the soil seems to be awaiting our pleasure." "The Chinese raise more per acre than is raised in the United States." One might cite other lands with a permanently high fertility. The conditions in the other countries are, however, different. The American farm crops are shipped to the cities, whence they find their way into the sewers, rivers, oceans and incinerators; the Chinese saves every bit of organic matter, and carries the "night soil" from the city to the farm. Furthermore, much of the permanency of fertility of certain regions of China is due to the recurrent fertility additions by fertile river mud. Similarly, the permanent fertility of the Nile Valley is due to the annual fertilization of the land by the Nile River.

Unlike Whitney, Bennet[12] is very pessimistic about American soil fertility, as indicated by the following quotation.

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[9] Hottel, H. C., *Sigma Xi Quarterly*, **29**, 49 (1941). "The solar power is not there for the taking! With respect to the future of solar energy utilization, your guess is as good as mine."

[10] *cf* Shepherd, G., "Power alcohol from farm products." *Contrib. Iowa Corn Res. Inst.*, **1**, 283 (1940): with corn at 50 cents per bushel, alcohol may be made for fuel blending purposes at 25 cents per gallon. If, however, we were to rely on alcohol as exclusive source of power for automobiles, the price of corn and alcohol would become very high indeed.

[10a] For a more optimistic view, see Berl, E., "Production of oil from plant material," *Science*, **99**, 309 (1944).

[11] Whitney, Milton, "Soil and civilization." New York, pp. 270, 272, 1925.

[12] Bennet, H. H., "Soil erosion and its prevention." Parkins, A. C. and Whitaker, J. R., Ed., "Our national resources and their conservation." New York, 1926. See also Bennet, U. S. Yearbook of Agriculture, p. 429, 1940, and U. S. Yearbook of Agriculture, 1938. See also, Duley, F. L., and Miller, M. F., "Erosion and surface run off under different conditions." Univ. Mo. Agr. Exp. Sta. Res. Bull., 63, 1923.

> Actual soil losses, as determined by exact measurements, are staggering. Approximately 50 million acres of once productive land has been ruined for crop use, and another 50 million acres is in almost as bad condition. Had it been protected, this aggregate 100 million acres divided into 80 acre farms would support 1,250,000 rural families.
>
> Something over 100 million additional acres, largely still in cultivation, has lost all or the greater part of its productive topsoil; on yet other millions of acres erosion is getting actively under way. About 470 million acres lost from $\frac{1}{2}$ to $\frac{3}{4}$ of the top soil.
>
> In addition to erosion losses, there are serious losses by cropping, grazing, and leaching. The latest estimates indicate the annual losses from these causes at approximately $1\frac{1}{2}$ million tons of phosphorous, 13 million tons nitrogen, 18 million tons potassium, 253 million tons organic matter.

The situation is even more discouraging to Stuart Chase, not a soil specialist but a very penetrating lay observer:[13]

> Before the coming of the machine, farm wastes and manures returned minerals to the soil at about the same rate as they were taken out. But under the deep, one-crop, commercial farming conditions, minerals go out of the soil to the cities and they never come back.
>
> A dust desert is forming east of the Rockies where firm grass once stood. The natural grass cover has been torn to ribbons by steel plows and cattle and sheep hoofs. Thousands of years of soil accumulation is lost in a century. Spindling woodlands cover only half the area the primeval forest once covered. Corn yields in sections of Iowa dropped from 50 to 25 bushels per acre. Half of the original fertility of the continent has been dissipated. American has achieved its high standards by living on its reserve capital, by taking more out of the continent than was put back.

There are historical parallels to our dust-bowl, dust-storm, migratory-worker problem in parts of Texas, Wyoming, eastern Colorado, western Kansas, and western Oklahoma. Thus, again from Chase:

> There were 400,000 people in the city of Antioch; the pleasure gardens of Daphne were famous throughout the Mediterranean world. Today it is a miserable dusty town of 30,000. Antioch perished not from its sins but from erosion on the Taurus and Lebanon rivers.

One might cite other thoughtful observers, especially on historical parallels to our situation. Thus from Sears:[14]

> The course of farm life and farm management in Rome ran from yeomanry to tenantry, and finally to holdings of absentee landlords. In spite of the exceedingly fertile lands of northern Italy, watered and nourished from the Alps, Rome entered upon a period of agricultural decline and could not feed her own people.

The following is from our former Secretary of Agriculture, H. A. Wallace:

> We overplow the cropland, overgraze the pasture land, overcut the timberland, plow fertility into cities, which in time pours down the sewers into the river and the ocean.

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[13] Chase, S., "Rich land poor land." McGraw Hill Book Co., pp. 20, 21, 34, 36, 37, 342.

[14] Sears, P. B., "Deserts on the march." University of Oklahoma Press, 1935.

It is true that: there is at present an apparent abundance of food; we can manufacture nitrogen fertilizers from the air; we can enrich soil with organic matter from nitrogen-rich legumes. Nevertheless, our machine-methods of cultivation will yield ever smaller crops in some regions, and in a few years, with the increased population living at a high standard, we shall need our land for food production, and it will not be possible to spare it for producing fuels as substitute for petroleum products and coal. We shall do well enough if we can supply food at a high standard to a population almost 200-fold that supported under the conditions of the American Indian 300 years ago. The decline in soil fertility, moreover, tends to reduce, or unbalance, the nutritive value of the crops that can be produced (see Sect. 20.8).

In brief, the phenomenal industrialization in the past century is based in part on borrowed capital and, one might say, borrowed time; capital and time accumulated in the past geologic ages. This capital is of two kinds: 1) petroleum fuel which is being rapidly exhausted, will perhaps be unavailable for ordinary use of private automobiles and tractors within a relatively short interval and coal which will last for a considerable period 2) soil which has also been severely exploited; but much of which, with proper care, will yield renewable vegetation energy perhaps indefinitely. A new source of permanent power is being harnessed productively, namely that of running water for generation of electricity. The other suggested power sources, such as conversion of solar energy to utilizable heat or electricity, or interatomic energy, are not promising.

This energetic viewpoint may be too pessimistic. We may find new energy sources. We may rebuild our soil losses and maintain our soil resources by turning our attention and imagination to the building up of the countryside instead of the cities.[15] Such a new optimistic development is exemplified by the TVA (Tennessee Valley Authority), indicated by the following quotations from former U. S. Senator George W. Norris.[16]

> Before the TVA, our fertile valleys were being depleted of their soil. . . . Annual floods swept through them at terrible cost. . . . Erosion was unchecked . . . and the swollen rivers carried . . . top soil down to the sea. The dams built by the TVA prevented flood damage, and also kept open navigable channels. A comparatively small additional sum enabled the Authority to utilize the waters impounded behind the great dams for the generation of huge amounts of electric power. This power has been carried into the homes of farmers and provided amenities they never knew before; it furnished cheap electricity to city dwellers; and in factories and industrial plants in the South it is contributing mightily to the war effort and bringing prosperity to the people.

---

[15] Hammar, C. H., "Society and conservation," *J. Farm Economics*, **24**, 109 (1942).

[16] Norris, George W., *The Nation*, May 20, p. 589, 1944, who also reviews W. C. Lowdermilk's recent book "Palestine, land of promise," Harpers, 1944. The author is Assistant Chief of the U. S. Soil Conservation Service, sent by the U. S. Department of Agriculture to study denudation and conservation of soil, especially in the Near East.

Then Norris quotes the suggestion for adoptation of the TVA plan for the establishment of a JVA (Jordan Valley Authority) for reclamation purposes as follows:

> Centuries ago Palestine was a prosperous country, covered with fertile fields of forests. Its fertility was destroyed by man's failure to conserve its natural resources. After Palestine was set aside as a Jewish homeland, it became a great experiment in reclamation. The Jews built cities and formed agricultural colonies and brought the soil back to abundant production. "It is practically impossible," says Dr. Lowdermilk,[16] "to estimate what the final absorption capacity of Greater Palestine could be if all its unoccupied and underpopulated areas were rejuvenated by the same vigor and understanding. . . ." Once the undeveloped resources (hydroelectric power developed from the rushing river down the Dead Sea, reforestation, mineral extraction) of the countries are properly exploited, twenty to thirty million people may live decent lives where a few million now struggle for a bare existence. The principle of the greatest good for the greatest number and the principle of preserving the natural resources of the country should lead to ever wider adoptation of the TVA principle, yes, even to developing a "TVA of the Danube," without regard to national boundaries, which would transform the economically backward Danube basin (Poland, Czechoslovakia, Austria, Hungary, Rumania, Yugoslavia, Bulgaria and Greece) into a prosperous one.

Senator Norris, however, presented only one aspect of the picture of the beneficent changes developed by modern science and technology. There is another aspect. According to the principle of population growth (Sect. 16.5), doubling the food supply merely doubles the population density without necessarily increasing its welfare. It has been predicted[17] that (because of developing science and technology and perhaps for military reasons) the U.S.S.R. will grow from the present 174 million to 251 million by 1975; India may grow from the present 389 million to 500; China from the present 400 million to 600 million. . . . "The fulfillment of the most sanguine hopes of science and industry for increasing the means of living will be inadequate if birth control does not become the rule in all the world."[17] Wars, however, "shake the biologic foundations of human life" and upset all predictions.[18]

25.3: Summary of summary.

> The analysis of the whole, as a whole, is as necessary as the analysis of parts. *R. S. Lynd*
>
> We suffer less from a want of science and technology than from lack of understanding of the aims of life and of society. *R. W. Hutchins*
>
> We are on the threshold of a new era. But what sort of an era? *Quo Tai Chi*

This book has been preoccupied with the quantitative aspects of energy and nitrogen metabolism, with nutrition, with various phases of growth, development and aging, with the catalysis of these processes, with the energetic efficiencies and profits on milk, meat, eggs, and muscular-work production, with generalizing equations—so-called laws—for integrating unwieldy bodies of data.

During this writing a need was felt for a generalizing or unifying principle, perhaps comparable to the principle of evolution, perhaps some broadly organismic theory or conceptual scheme which would show by a word or phrase the interrelatedness of all the components of the field that we have been considering.

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[17] Thompson, W. C., "Plenty of people," Jacques Cattell Press, 1944.

[18] Birth rates in warring countries," Editorial, *Jour. Am. Med. Assn.*, **125**, 278 (1944).

The ancient,[19] perhaps vaguely felt, concept of physiological regulation ("The organism acts as though it desired to maintain itself" C. Sherrington) scientifically investigated since about 1860 (Claude Bernard), and recently designated homeostasis by Cannon (Sect. 10.11), comes nearest to meeting the need of a broadly unifying principle if its meaning is extended to include social self-regulation, including that of human society (Sect. 10.9). Senescence, disease, individual and social catastrophe, are due to or characterized by failure of homeostasis. Under condition of failing social homeostasis, subhuman animals are doomed. The sabretoothed tiger had to disappear because it developed his magnificent sabre-teeth weapons which tempted him to war-like action. On a human level, however, we may, perhaps, discover methods for preventing catastrophe in the face of our splendid weapons which tempt us to destructive wars, and our wonderful machines which consume our stockpile of "free energy" and our soil resources at ever greater rates.

The current confusions and maladjustments may be transitory, temporary disharmonies associated with rapid growth, in the nature of "growing pains," which may be resolved into a harmonious unity. But this is not certain. The future trends of human behavior are not predictable[20] because human behavior is modifiable by intelligence, by education, by laws of human making in contrast to the immutable natural laws which govern the social trends of subhuman populations. This relative indeterminacy of human behavior and social phenomena is the despair of the social scientist and perhaps the hope of humanity; for this gives man an opportunity to mold his destiny that is not given to other species that are subject to more determinate, orderly, laws. There is more than poetic significance to the biblical assertion that "The Kingdom of Heaven is within you." The major contemporary problem is how to employ science for guiding individual and social development so as to realize this Kingdom of Heaven on earth[21].

---

[19] "The preservation of health depends on a proper balance of forces."—Alcmaeon, 460 B.C. (Quoted from Adolph, E. F., "Physiological regulations," Cattell Press, 1942.) For Bernards' classic exposition, see Bernard, C., Leçons sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme. Paris, Baillière, 1859. See also Cannon, W. B., The wisdom of the body. New York, Norton, 1932.

[20] Frank, L. K., "The principle of disorder and incongruity in economic affairs," Political Sc. Quarterly, Dec. 1932, and *Sci. Monthly*, **50**, 49 (1940).

[21] Brody, S., "Science and social wisdom." *Sci. Monthly*, **59**, 209 (1944).

CONVERSION FACTORS[1]

Acre = 0.4047 hectare
= 43,560 sq. ft.
= 4046.9 sq. meter

Angstrom = Å
= 0.001 micron
(mu or μ)

Atmosphere pressure
= 760 mm. Hg
= 29.92 in. Hg
= 10.33 meters water
= 33.9 ft. water
= 1033.3 gm./sq. cm.
= 14.7 lb./sq. in.
= 2116.3 lb./sq. ft.

Barrel = 31.5 gal.
= 126 qt.
= 119 liter

Bushel = 32 qt.
= 77.7 lb. water
= 35.2 kg. water

Can: #1 tall = 1 lb.
#2 = 1 lb. 4 oz.
#2½ = 1 lb. 12 oz.
#3 = 2 lb. 2 oz.
#10 = 6 lb. 10 oz.

Centimeter = 0.01 meter
= 0.3937 in.

Cm^2 = 0.155 sq. in.

Cm^3 = cc. = ml.
= 0.061 cu. in.
= 1 gm. water
= 0.0353 oz. water
= 15.432 grains water
= 12 drops

Cup = 0.5 pint
= 16 tablespoons
= 24 dessert spoons
= 48 teaspoons

Dessert spoon
= ⅔ tablespoon
= 2 teaspoons
= 120 drops

Foot = 30.48 cm.
= 0.3048 meter

Ft^2 = 144 sq. in.
= 929.0 sq. cm.

Ft^3 = 7.4805 gal.
= 29.922 qt.
= 28.32 kg. water
= 28.32 liter water
= 62.43 lb. water
= 999 oz. water

Gallon = 4 quarts
= 3.785 liters
= 8.345 lb. water
= 3.785 kg. water

Gram = 0.035274 oz.
= 0.002205 lb.
= 15.432 grains

Hectare
= 2.471 acres
= 10,000 sq. meters
= 107,638.7 sq. ft.

Inch = 2.54 cm.
$\frac{1}{10}$ in. = 2.54 mm.

In^2 = 6.4516 cm.^{2}

In^3 = 16.387 cm.^{3}
= 0.0346 pt.
= 0.0164 liters
= 16.39 gm. water
= 0.578 oz. water
= 0.0361 lb. water
= 252.89 grain water

Kilogram = 2.205 lb.
= 35.274 oz.

Liter = 0.26418 gal.
= 1.0567 qt.
= 35.275 oz. water
= 2.205 lb. water
= 1 kg. water

Meter = 3.2808 ft.
= 39.37 in.
= 1.0936 yd.

M^2 = 1.2 sq. yd.
= 10.764 sq. ft.
= 1550 sq. in.
= 10,000 sq. cm.

M^3 = 1000 liters
= 1056.7 qt.
= 35.31 cu. ft.
= metric ton water
= 2204.6 lb. water

Microgram = mcg. = μg
= γ = gamma
= 0.001 mg.

Mile = 5,280 ft.
= 1609.4 meters
= 1.6094 km.

Mile^2 = 640 acres
= 2.59 sq. km.

Milligram = 1000 mcg.

Millimeter = 1000μ (or mu)
= 10,000,000 Å

Ounce = 28.3495 gm.
= 0.0625 lb.
= 437.5 grains

Pint = 0.5 qt.
= 473.18 cc.
= 16.69 oz. water
= 1.043 lb. water
= 0.47318 kg. water
= 2 cups
= 32 tablespoons
= 96 teaspoons

Pound = 16 oz.
= 453.6 gm.
= 0.4536 kg.

Quart = 2 pt.
= 4 cups
= 946.4 cc.
= 64 tablespoons
= 192 teaspoons
= 33.38 oz. water
= 2.086 lb. water
= 0.946 kg. water

Tablespoon
= 0.0625 cup
= 15 cc.
= 1.5 dessert spoon
= 3 teaspoons
= 180 drops

Teaspoon = 5 cc.
= 0.02 cups
= 60 drops

Temperature conversion:

$$^\circ\text{C.} = \frac{^\circ\text{F.} - 32}{1.8}$$

$$^\circ\text{F.} = (^\circ\text{C.} \times 1.8) + 32$$

Ton: short ton = 2000 lb.
long ton = 2240 lb.
metric ton = 1000 kg.
= 2204.6 lb.

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[1] See pages 35 to 36 for energy, work and dietary units, and page 766 for vitamin units.

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